STRATEGIC PROGRAM PLAN

Space Radiation Health

NASA

FOR SPACE RADIATION HEALTH RESEARCH

Strategic Program Plan
for
Space Radiation Health Research

Life Sciences Division
Office of Life and Microgravity Sciences and Applications

The attached document is NASA's Strategic Program Plan for Space Radiation Health Research. This document has received extensive review. It was distributed to the management of Codes U, UG, and UL and to the members of the Radiation Coordination Team at NASA Headquarters and to the Lead Center, Johnson Space Center. Also, 100 copies were distributed at the Ninth Annual Space Radiation Health Investigators' Workshop, held June 14–17, 1998, in Loma Linda, California. The resulting comments have been incorporated into the current version.

The present document supersedes the program plan approved by the Life Sciences Division Program Requirements Control Board on December 2, 1991. Authority for establishing and implementing the policies and procedures required by this Strategic Program Plan is vested with the Director of the Life Sciences Division.

Approved:

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10 / 16 / 98	10/23/98
Date	Date

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Radiation Quantities

Absorbed Dose D: average energy absorbed per unit mass of any material
- – units: Gray (Gy) = 1 Joule (J)/kg (= 100 rad)

Fluence (F): number of incident particles per unit area (on a sphere)

Linear Energy Transfer (L or LET): the amount of energy absorbed locally, per unit path length, when a charged particle traverses tissue
- – units: keV/µm

Quality Factor (Q): a weighting factor for dose, proportional to the estimated risk per unit dose (different for different types of radiation)

Dose Equivalent H: estimate of radiation risk
- – $H = QD$
- – the same dose has different biological consequences in different tissues for different radiation types
- – common risk scale for different doses (Q = 1 for x-rays)
- – units: Sievert (Sv) (= 100 rem)

Effective Dose E (ICRP 60): estimate of radiation risk
- – $E = \Sigma\,\Sigma\,w_R\,w_T\,D_{T,R}$ ($D_{T,R}$ = average dose from radiation R in tissue T; w_R = radiation weighting factor; w_T = tissue weighting factor)
- – units: Sievert (Sv) (= 100 rem)

Relative Biological Effectiveness (RBE) for a specific end-point: the ratio of doses required to achieve the same end-point
- – RBE (other radiation) = D (x-rays)/D (other radiation)

Cross Section σ: probability per unit particle fluence of observing a given end point; radiation risk is proportional to fluence:
- – Probability (given end point) = $\sigma\,F$
- – units of σ: cm^2

Energy (per Nucleon) ε: for an energetic atomic nucleus consisting of neutrons and protons ("nucleons"), the kinetic energy of the nucleus divided by the number of nucleons (atomic number A); for a neutron or proton, the kinetic energy of the neutron or the proton
- – units of ε: kilo-, mega-, giga-electron volt per nucleon (keV/A, MeV/A, GeV/A)
- – the kinetic energy of the HZE nucleus of atomic mass A is ε A (keV, MeV, or GeV)
- – one electron volt (= 1.6×10^{-19}J) is the energy gained by an electron in passing through a potential difference of 1 volt

RADIATION QUANTITIES

AGS	Alternating Gradient Synchrotron
ALARA	as low as reasonably achievable
BAF	Booster Applications Facility
BNL	Brookhaven National Laboratory
EVA	extravehicular activity
GCR	galactic cosmic rays
Gy	Gray (unit of absorbed dose, 1 J/kg)
HZE	the component of galactic cosmic rays consisting of high-energy (high-E) nuclei of heavier (high atomic number Z) elements
ICRP	International Commission on Radiological Protection
ISS	International Space Station
LEO	low-Earth orbit
LET	linear energy transfer
NAS	National Academy of Sciences
NRC	National Research Council
NSBRI	National Space Biomedical Research Institute
NSCORT	NASA Specialized Center of Research and Training
OLMSA	Office of Life and Microgravity Sciences and Applications
OSHA	Occupational Health and Safety Administration
SAA	South Atlantic Anomaly
SPE	solar particle event
STS	Space Transportation System (Space Shuttle)
Sv	Sievert (unit of dose equivalent)

1. Introduction

Space radiation has a major impact on all NASA activities:

- Legal, moral, and practical considerations require that NASA limit the postflight risks incurred by humans living and working in space to "acceptable" levels.

- Radiation protection is essential to enable humans to live and work safely in space.

- Proper strategies for implementing radiation limits applicable to crews and frequent users of high-flying aircraft need to be devised.

- Electronics and instruments in space need to be operated in a manner independent of radiation-induced failure modes.

- Space science instruments need to be developed or improved and calibrated for proper interpretation of observations.

- The effects of space radiation on long-term life support systems (plants as well as electronics) need to be mitigated.

- The role of radiation in the evolution of life needs to be understood.

- The interaction of radiation with hypogravity needs to be understood to discriminate between the biological effects of weightlessness and the effects of radiation.

These facts have been recognized for a long time. They have become of critical importance for several reasons:

- The advent of the International Space Station (ISS) makes imminent a long-term human presence in space.

- With the advent of the Space Station, NASA must prepare for the next step beyond the horizon: human space exploration, including a return to the Moon, and human exploration of Mars and, perhaps, extraterrestrial moons or asteroids.

- The revolution in radiation biology that has occurred in the last 10 years for the first time makes scientific approaches and breakthroughs conceivable that could dramatically alter our ability to predict and manage radiation risk.

- Our understanding of the physical sources of space radiation risk and their interactions with matter has progressed to the point where substantial advances can be expected.

- New technology developed over the past decade can now be exploited to monitor, shield, and validate radiation predictions in space.

1.1 Predicting Radiation Risk

The components of space radiation that are of concern are high-energy, charged particles, especially the component of galactic cosmic rays consisting of high-energy (high-E) nuclei of heavier (high atomic number Z) elements ("HZE particles"). NASA is concerned with two main types of radiation risk:

1. Short-term consequences of relatively high levels of radiation, such as might be caused by a solar particle event (SPE) or even repeated exposure during passage of the South Atlantic Anomaly, are a type of radiation risk that is main-

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ly caused by cell depletion of sensitive tissues, such as the bone marrow, intestinal epithelium, skin, or may lead to symptoms affecting the health and performance of crews.

2. Long-term exposure to expected levels of solar and galactic cosmic radiation results in an enhanced probability of cancer and, possibly, changes in the cells of the brain, reproductive organs, or other tissues.

Predictions about the nature and magnitude of these risks are subject to very large uncertainties. The magnitude of these uncertainties is difficult to estimate and depends on the type of risk and the models used for risk prediction. Prudent use of worst-case scenarios based on large uncertainties leads to excessive engineering margins. Such margins may impose unacceptable constraints on shielding mass for spacecraft or habitats, tours of duty of crews on the ISS, and the radius and duration of sorties on planetary surfaces.

1.2 Countermeasures

Countermeasures are approaches to mitigate risk. There are five possible approaches, but only the first two of these are currently practical and cost-effective. The five approaches are:

Operational. The time of exposure and the duration of exposure should be limited by various strategies, such as selecting older crew members, avoiding EVA's during passage through the South Atlantic Anomaly, using spacecraft transfer trajectories that minimize the duration of interplanetary travel, and so forth.

Shielding. Much progress has been made by scientists supported by the Life Sciences Division. Data on

the galactic cosmic radiation environment is now estimated to be accurate to within ±15 percent. An initial data set of shielding properties of conventional and new materials has been obtained and found to be within ±50 percent of calculated values. Computational tools have been developed to calculate how incident radiation is modified at any depth in materials; these tools have become the standard engineering method for estimating spacecraft shielding. The instrumentation necessary for completing the data base has been developed and is operational, and a cadre of world-class scientists has been assembled for this work.

Screening. It is well known that some individuals have genetic predispositions resulting in a higher cancer risk than normal. Procedures to screen for radiation susceptibility (or, if it can be demonstrated, abnormal radiation resistance) are currently of limited usefulness. Complicating the issue are questions related to the proper course of action to follow if testing reveals higher cancer susceptibility and whether aggressive surveillance of such individuals, if they elect to continue working in a space radiation environment, is warranted or even beneficial.

Prevention. Current knowledge of substances useful for radiation protection is limited. Pharmaceuticals can be used as radioprotectants for planned radiation exposures, but they have serious side effects and may not be useful for protection against HZE particles. Genetic methods to enhance the organism's ability to repair radiation damage (a "radiation vaccine") may be conceptually possible but beyond the horizon.

Intervention. This may be required to address prompt radiation effects arising, for example, from high radiation levels caused by solar disturbances. Biomolecular intervention after radiation exposure

may be possible in the future, perhaps using gene therapy methods to enhance cell repair or inspect damaged cells and induce programmed cell death in them.

1.3 Space Radiation Health Program

The NASA Space Radiation Health Program has been devised to develop the data base and the knowledge required by NASA to accurately predict and to efficiently manage radiation risk.

- The knowledge, once acquired, is available "forever" as part of NASA's intellectual capital.

- The knowledge will be acquired by means of a peer-reviewed, largely ground-based and investigator-initiated, basic science research program.

- Space-based experiments will be used to validate predictions of the basic science program and to acquire data that can uniquely be obtained in space.

- The knowledge will be integrated into models developed under NASA direction that will provide accurate risk predictions for the ISS and eventual exploration of deep space.

- Advanced technology development, sponsored by NASA, will lead to countermeasures that prevent, mitigate, and ameliorate possible deleterious effects of radiation.

The Life Sciences Division in the Office of Life and Microgravity Sciences and Applications (OLMSA) at NASA Headquarters has been charged with the development of this Strategic Plan and oversight of its implementation. The Division will be responsible for research solicitation and selection. The Division will continue to seek leverage of national and international resources. This includes coordination with representatives of all NASA programs handling radiation effects, with other Federal agencies that sponsor research applicable to the NASA mission, and ongoing efforts to engage our international partners. Relevant memoranda of understanding with related organizations are listed in Table I.

Table I. Agreements With Others

Organization	Date

Department of Energy
    Memorandum of Understanding
    Brookhaven National Laboratory
    Implementation Agreement
	July 9, 1990
	April 13, 1994
	October 29, 1997

Defense Nuclear Agency (AFRRI)	November 9, 1990
NASA/DARA	February 1992
National Cancer Institute	July 1, 1994
High Speed Research Division (RH)	November 2, 1994
Loma Linda University	December 1, 1994

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Johnson Space Center, in the role of Lead Center, will manage the implementation of this program. The Lead Center will produce an Implementation Plan, for Headquarters approval, to guide the implementation of the initiative. Implementation will include responsibility for integrating the basic science results into engineering tools suitable for predicting and managing risk on the ISS and for deep space exploration missions. The Lead Center also will implement risk management by developing and obtaining approval for flight rules to limit radiation exposure in accordance with guidelines provided by the National Council on Radiation Protection and Measurements (NCRP) and the "as low as reasonably achievable" (ALARA) principle to which NASA is legally committed.

This document outlines the Strategic Plan for the Life Sciences Division to address and solve the space radiation problem in a manner consistent with the high priority assigned to the protection and health maintenance of crews. This Plan is an organic evolution of the Space Radiation Health Program Plan approved in November 1991 by the Life Support Branch, Life Sciences Division, and Office of Space Science and Applications. It is based on principles set down by the Associate Administrator for OLMSA. It defines the goals and how they fit into the Human Exploration and Development of Space (HEDS) Enterprise Strategic Plan—the elements of the program, the mission, the deliverables, and the management strategy. Further information on the genesis of this Plan may be found in Appendix A. Radiation limits for crew exposures in space and their impact on this program are discussed in Appendix B.

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2. Vision/Purpose

Achieve human exploration and development of space without exceeding acceptable risk from exposure to ionizing radiation.

3. Mission

- Understand and quantify the space radiation environment

- Understand and quantify radiation risk

- Reduce or prevent impact of radiation risk

4. Program Description and Approach

4.1 Radiation Within NASA Strategic Management

In the NASA Strategic Plan, the NASA Administrator sets forth the direction for individual programs to follow. With respect to the radiation problem, Administrator Daniel Goldin states (emphasis added): "In implementing our mission, we will pursue answers to *fundamental questions of science and research* that provide a philosophical underpinning for why NASA exists and a foundation for our goals."

These fundamental questions include the following question: "What is the fundamental role of gravity and cosmic radiation in vital biological, physical, and chemical systems in space, on other planetary bodies, and on Earth, and how do we apply this fundamental knowledge to the establishment of permanent human presence in space to improve life on Earth?"

The strategy to be followed by the Space Radiation Health Program, in the context of the NASA Strategic Plan, is outlined in Figure 1, where its objectives are summarized. The strategy to be followed is simple: use the fact that space radiation can, to a large extent, be simulated in ground-based laboratories to acquire fundamental data and develop models for risk prediction. To the greatest extent possible, these models are based on fundamental scientific knowledge of the mechanisms of radiation action and not on phenomenological or empirical approaches. With well-defined theories, uncertainties can be estimated and acquisition of significant data can be specified to obtain major improvements in accuracy. An adequate scientific

basis will also lead to the design of biological methods of prevention and intervention to mitigate radiation damage. The science has important spinoffs, most notably in the treatment of cancer.

4.1.1 Performance Goals

- Determine the biological factors that contribute to risk

- Simulate space and planetary radiation environments with proton and heavy ion beams at ground facilities

- Develop methods to determine tissue and organ doses

- Develop radiobiology telescience and advanced sensors

4.1.2 Key Milestones/Products

- Prediction of risk for acute effects (bone marrow, lymphopoietic tissue, gonadal tissues, intestinal epithelium, skin)

- Prediction of risk for late effects (cancer-related lethality, incidence, impairment of fertility, lens opacifications, CNS, genetic damage)

- Biologically effective shielding design requirements

- Biomolecular methods for prevention and intervention of radiation damage

4.1.3 Major Assumptions

- Ground-based research program using high-energy, heavy-ion beams at Brookhaven

PROGRAM DESCRIPTION
AND APPROACH

Figure 1. Space Radiation Health Program and NASA Strategic Plan

Agency Mission	1998–2002	2003–2009	2010–2023	Contributions to National Priorities
To advance and communicate scientific knowledge and understanding of Earth, the solar system, and the universe and use the environment of space for research	Model space radiation environment, especially trapped radiation; measure ISS radiation environment	Measure radiation on surface of Mars	Develop and deploy operational strategies for managing solar particle event risk	Contribute to increased understanding of solar physics; contribute to reliable space instrumentation technologies
To explore, use, and enable the development of space for human enterprise	Use accelerator-based beams to simulate the space radiation environment; predict acute risk during SPE; radiation dose limits on the ISS	Continue accelerator work; set astronaut radiation dose limits for exploration; optimize shielding design	Finish accelerator work; develop diagnostics of radio-sensitivity and gene therapy for prevention and/or treatment of radiation damage	Design exploration missions; safe operation of the ISS
To research, develop, verify, and transfer advanced aeronautics, space, and related technologies	Joint NASA-NCI research in carcinogenesis; measure HZE risk of damage to the central nervous system in mammalian animal models	Complete data base and modeling to predict galactic cosmic ray risk; develop radiobiology telescience for remote experiments on the ISS and precursor missions	Validate radiation risk predictions in space on the ISS and precursor missions; understand synergies with hypogravity	Apply to diagnosis, prevention, and treatment of cancer on Earth; apply radiobiology telescience to high-risk Earth environments

National Laboratory (BNL) and proton beams at Loma Linda University Medical Center to simulate space radiation

- Program supplemented with heavy-ion beams at Darmstadt, Germany, and Chiba, Japan

- Funding for construction and operation of Booster Applications Facility (BAF) at BNL in NASA budget

- Funding for expansion of research community and continued participation of the research community in NASA budget

4.2 Roadmap

A roadmap for accomplishing the program vision of assuring a permanent human presence in space is shown schematically in Figure 2. Our limited basic knowledge required to answer the critical questions

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is obscured by uncertainties. To acquire the necessary basic knowledge and reduce uncertainties in risk prediction, the strategies to be followed are: (1) simulate space radiation on the ground, where studies can be performed most cost-effectively; (2) take advantage of available space platforms, such as robotic precursor missions; (3) validate predictions based on ground-based science on the ISS and other space platforms (for example, the Space Shuttle) to determine the interaction of radiation with weightlessness; and (4) develop countermeasures to radiation risk.

The results of this program will be used to develop risk management tools for the ISS as well as for deep space exploration. Risk management under ALARA requires that action levels be established at radiation exposures that are well below the maximum permissible limits.

Action levels are required at the design stage of space missions as well as during mission operations. At the design stage, the program will provide requirements for warning and forecasting, tools for the optimization of shielding, and resources for the implementation of biomedical countermeasures. Operational decisions are implemented by means of *flight rules* that specify radiation monitoring and personnel dosimetry, responses to unplanned radiation exposures (for example, during a solar dis-

Figure 2. Space Radiation Health Program Roadmap

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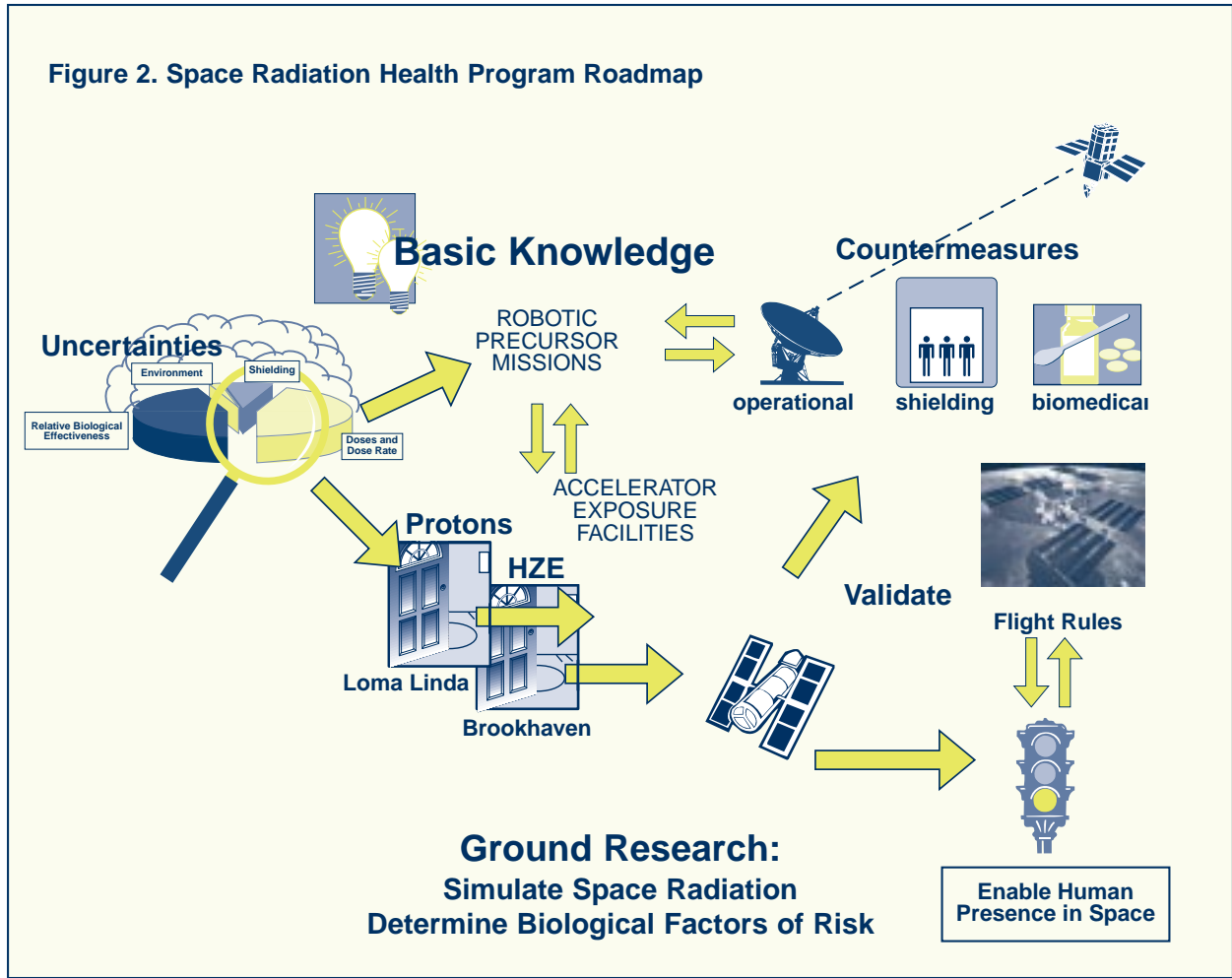
turbance), responses to radiation monitoring and warning, scheduling of EVA, tours of duty, and so forth.

Several parts of the roadmap are discussed in further detail in the Appendices to this document:

- The uncertainties that cloud our current knowledge and that may result in unacceptable worst-case designs, are discussed in Appendix C.

- The basic knowledge that is required consists of knowledge about the space radiation environment (Appendix D), the interaction of space radiation with matter (Appendix E), and the biological consequences of this interaction (Appendix F).

- Elementary notions of shielding, based on information provided by physics and biology, are given in Appendix G.

- A list of critical questions in support of humans in space was developed in 1992 by the Aerospace Medicine Advisory Committee of the NASA Advisory Council; the questions pertaining to radiation, with a few subsequent additions, are listed in Appendix H.

- The specifications for ground-based research facilities that simulate space radiation are discussed in Appendix I. They lead to the conclusion that only one currently operating facility, at Brookhaven National Laboratory in New York, can satisfy the scientific requirements for ground-based research with HZE particles. This facility must be complemented by a facility providing proton beams. The only facility available in the United States where proton beam studies can be conducted in a biomedical research environment is the Proton Therapy Synchrotron at Loma Linda University in California.

5. Elements

5.1 Simulate Space and Planetary Radiation Environments

Construct and operate ground facilities at Brookhaven and Loma Linda University Medical Center

5.2 Acquire Essential Biomedical Data

Ground Research

- Answer critical questions developed by the scientific community
  - Propagation of radiation through matter (radiation transport)
  - Carcinogenesis
  - Central nervous system effects

- Develop genetic screening

- Predict biological effects of protons and HZE components of space radiation
  - Update radiation limits for long-term radiation effects

- Conduct clinical research—treatment in case of exposure: pharmacological/genetic

Space Research

- Support efforts that may lead to increased ability to forecast and characterize SPE with adequate response times and low false alarm rates
  - Update radiation limits for prompt radiation effects

- Coordinate emergency medical response for unplanned exposures (for example, during EVA)

- Coordinate international agreements on managing radiation risk on ISS

- Provide measurements of the space radiation environment (monitoring and dosimetry)
  - Robotic precursor missions
  - Shuttle and Station dosimetry

- Validate ground-based model predictions

- Utilize the ISS to establish interaction between radiation and hypogravity effects

5.3 Develop Shielding Materials

Ground Research

- Determine shielding properties of novel materials

- Incorporate biological effects of protons and HZE particles into the biological characterization of shielding

Space Research

- Validate ground-based model predictions

5.4 Incorporate Biomedical and Materials Requirements Into Mission Design

- Standardized mission design tools (radiation transport, dosimetry, and so on)

- International protocols based on ALARA for dose measurements and monitoring

- Strategy to develop, review, accept, and implement flight rules

- Emergency response procedures for unplanned radiation exposures

6. Deliverables

6.1 Program Phases

The delivery of program products has been phased in accordance with the time scales of the NASA Strategic Plan. The Space Radiation Health Program is divided into three phases, covering short-term, intermediate-term, and long-term progress. The program is expected to be completed before 2023, at which point all the products will have been transferred to operational organizations.

In each phase, deliverables have been identified, and priorities assigned, based on the readiness and the likelihood of progress for each of the program elements listed above. For example, ground-based facilities to simulate the space environment can and must be utilized immediately to maintain their availability; experiments to exploit current biological knowledge and develop a shielding data base are in progress and can easily be expanded to yield immediately useful results. On the other hand, countermeasures based on biomolecular methods (for example, gene therapy), while currently conceivable, are, at this time, over the horizon, and they will require one or more research breakthroughs before they can be considered for application.

6.1.1 Phase 1, 1998–2002

This phase is intended to exploit currently available science to identify risks accurately. As discussed in Appendix A, the uncertainty in identifying risks places an enormous cost burden on current engineering approaches attempting to make worst-case designs and on flight rules intended to maintain radiation exposure within limits of acceptability. This uncertainty is a career-limiting factor for space

crews. The priorities of this phase are: (1) identify all risks from space radiation; (2) provide accurate estimates of uncertainty in risk prediction; and (3) lay the scientific and biomedical groundwork for significant reductions in uncertainty and the development of radiation countermeasures in the intermediate and longer term.

6.1.2 Phase 2, 2003–2009

The priorities of this phase are: (1) achieve significant reductions in the uncertainty of risk prediction; (2) complete the radiobiological data base for effects of HZE particles at energies in the range 50–600 MeV/nucleon; and (3) begin validation of ground-based risk prediction in space by ISS utilization.

6.1.3 Phase 3, 2010–2023

This phase is intended to fully develop biomedical science and technology for radiation risk mitigation and to take advantage of scientific breakthroughs expected to lead to practical biomolecular radiation countermeasures. The priorities of this phase are: (1) reduce the uncertainty of overall risk prediction to be no greater than ±50 percent; (2) extend the existing data base to develop effective radiation countermeasures; and (3) assure radiation risk management for deep space exploration missions. The research and development phase of this program is expected to end some time before the conclusion of phase 3, and radiation risk management will become an operational crew health care responsibility.

6.2 Breakthrough Strategy

Research breakthroughs, especially in the fast-moving science and technology areas of biotechnology, have occurred at a fast pace in recent

years. Examples of relevant breakthroughs within the last 15 years are the discovery of cancer susceptibility genes for which genetic testing is available, such as the hereditary retinoblastoma gene, the breast cancer genes BRCA1 and BRCA2, and some types of colon cancer, and a gene that is involved in susceptibility to cancer development and is associated with radiation sensitivity—the ataxia telangiectasia (AT) gene. Signal transduction pathways link cellular communication systems and result in altered gene expression and altered cellular phenotypes; new information on such pathways is being obtained on an almost daily basis. One of the major breakthroughs in recent years has been the discovery of mechanisms associated with the p53 gene, including apoptosis or programmed cell death. Modulation of the cell cycle in mammalian cells by cyclin-dependent kinases and, in general, an understanding of DNA damage checkpoints at the phase boundaries of the cell cycle have drastically improved our understanding of the response of cells to radiation.

For this reason, the product delivery schedule is based on a breakthrough strategy, where the implicit assumption is that research breakthroughs are expected to continue to occur at a regular rate.

The implications of this strategy are shown schematically in Figure 3.

The current uncertainty is shown as a factor of 10, based on the discussion of Appendix C, and the desired uncertainty goal is shown as ±50 percent. The current rate of progress, based on the NAS/NRC report, is assumed to have a half-life of approximately 30 years. At this rate, the uncertainty can only be reduced to be approximately 5 during the life of the program, well above the goal.

Doubling the current rate of progress leads to a half-life of 15 years. At this rate, the predicted risk, at the end of the program, would still be uncertain by a factor of 3 (that is, three times larger or smaller than the actual risk). Even tripling the rate of continuous improvement results in reducing the uncertainty to slightly less than a factor of 2.

These are significant reductions in current uncertainties, and a factor of 2–3 may already be considered acceptable. However, given the current progress in biology, it is realistic to assume that at least one significant breakthrough, leading to a reduction in uncertainty by one-half, is likely to occur every 5 years. With this assumption, the goal of an overall uncertainty equal to ±50 percent can easily be reached within the life of the program at a 15-year rate of continuous improvement. The implementation of this Plan will require a determination of the level of effort required to sustain the improved rate of progress. In addition, incentives and support must be provided for leveraging expected breakthroughs in science and technology and adapting them to the program objectives.

Figure 3. Breakthrough Strategy

DELIVERABLES
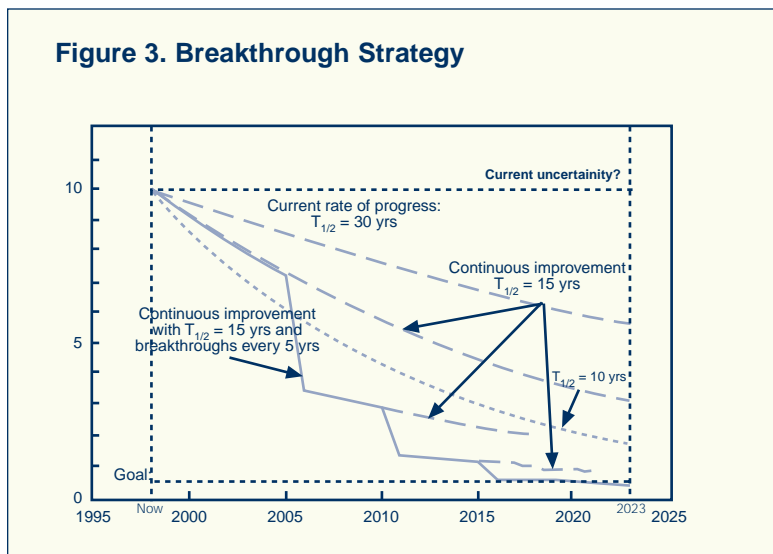
6.3 Facilities

6.3.1 Phase 1, 1998–2002

- Operation of AGS for approximately 600 hours per year

- Operation of Loma Linda University proton facility for approximately 400 hours per year

- Construction of BAF facility

- Collaborative research at HIMAC for approximately 100 hours per year

- Develop plans for collaborative research at GSI

- Develop plans for collaborative research with other interested international partners

6.3.2 Phase 2, 2003–2009

- Commissioning of BAF facility

- Operation of BAF for 1,000–2,000 hours per year

- Continue operation of AGS for 300–600 hours per year

- Operation of Loma Linda University proton facility for approximately 400 hours per year

- Collaborative research at HIMAC for approximately 100 hours per year

- Collaborative research with other interested international partners

- Use of centrifuge(s):
  – Ground-based to assess effects of hypergravity

  – ISS for controls of flight experiments
  – Radiation source(s) for ISS

6.3.3 Phase 3, 2010–2023

- Continued operation of BAF for 1,000–2,000 hours per year

- Operation of Loma Linda University proton facility for approximately 400 hours per year

- Collaborative research at HIMAC for approximately 100 hours per year

- Collaborative research with other interested international partners

- Use of centrifuge(s):
  – Ground-based to assess effects of hypergravity
  – ISS for controls of flight experiments
  – Space-based platforms for validation of risk predictions (ISS, Bioexplorers, other precursor missions)
  – Radiation source(s) for ISS

6.4 Space Radiation Countermeasures

6.4.1 Phase 1, 1998–2002

- Models of space radiation environment
  – Trapped radiation, especially in the ISS orbit
  – Near Mars environment

- Revised radiation limits for the ISS
  – Flight rules for the ISS
  – Emergency medical procedures for unplanned radiation exposures

- Monitoring and dosimetry on the ISS
  - Intercomparison and intercalibration with international partners
  - Establishment of international standards

- Initiation of biological countermeasure studies
  - Assessment of the possible use of radioprotectants for proton exposures

6.4.2 Phase 2, 2003–2009

- Validation of models of space radiation environment
  - Trapped radiation, especially in the ISS orbit
  - Shielding properties of Martian soil and atmosphere

- Storm shelter design for deep space exploration missions

- Continued monitoring and dosimetry on the ISS
  - Intercomparison and intercalibration with international partners
  - Establishment of international standards

6.4.3 Phase 3, 2010–2023

- Informed by human risk models

- Preventive biological countermeasures
  - Understanding of mechanisms, including age and time (pre- or postirradiation) dependence
  - Biodosimetry/biomarkers of radiation susceptibility and postflight risks
  - Radiosensitivity diagnostics and crew selection

- Intervention countermeasures
  - Postexposure genetic techniques (enhance repair/eliminate damage)

- Chemical and biological modifiers (cell cycle control, modifiers of gene expression, apoptosis, cytokines, and so on)

- Testing and validation on animal models

- Interactions with space flight factors

- Medical procedures
  - Acute effects (autologous bone marrow transplants, use of radioprotectors)
  - Requirements for medical response to unplanned space radiation exposures technology transfer (for example, clinical applications)

6.5 Mission Design Optimization

6.5.1 Phase 1, 1998–2002

- Shielding design tools
  - Radiation transport models for physical characterization of radiation fields inside arbitrary shielding distributions, tissues, and organs
  - Engineering versions for distribution

- Validation of radiation transport calculations
  - For high-energy protons (including nuclear interactions)
  - For selected HZE particles (hydrogen, helium, carbon, silicon, argon, magnesium, and iron nuclei) above approximately 600A MeV to take advantage of AGS availability

6.5.2 Phase 2, 2003–2009

- Definition of strategies for management of SPE
  - Implementation of solar monitoring, warning, and forecasting
  - Revised flight rules for SPE on the ISS and deep space exploration

- Radiation analysis of baseline exploration mission
  - Biological characterization of radiation transport radiation fields
  - Methods and mission trade studies
  - Requirements for in situ resource utilization
  - Radiation optimization of mission designs

- Validation of radiation transport calculations for low-energy HZE (hydrogen, helium, carbon, silicon, argon, magnesium, and iron nuclei in the energy range 50–600 MeV/nucleon) after commissioning of BAF facility

6.5.3 Phase 3, 2010–2023

- Optimized design for piloted deep space exploration mission
  - Optimized shielding distributions
  - Shielding designed for transfer orbits and planetary surface habitats

- ALARA-compliant flight rules established for deep exploration mission
  - Implementation of operational strategies for managing SPE risk (warning, forecasting, and monitoring)

6.6 Risk Prediction

6.6.1 Phase 1, 1998–2002

- Probability of risk for acute effects of protons
  - Accuracy: factor of ±200 percent

- Probability of risk for late effects of protons and HZE above approximately 600A MeV (cancer lethality, incidence, CNS) based on AGS experiments
  - Uncertainty in RBE-dependent components of risk model: ±200 percent

- Results of joint NASA/NCI research into mechanisms of genomic instability
- Results of molecular and cellular biology research for protons and for selected HZE particles (hydrogen, helium, carbon, silicon, argon, magnesium, and iron nuclei) above approximately 600A MeV to take advantage of AGS availability
- Unknown effects identified or ruled out

- Modeling of integrated results of environment, shielding, and radiobiology
  - Reliable estimates of uncertainty

- Resolution of bioethics issues (acceptable risk)

6.6.2 Phase 2, 2003–2009

- Probability of risk for late effects of protons and HZE particles in the BAF energy range 50–600 MeV/nucleon (cancer lethality, incidence, CNS)
  - Uncertainty in RBE-dependent components of risk model: ±50 percent
  - Results for in vivo studies
  - Unknown effects identified or ruled out

- Modeling of integrated results of environment, shielding, and radiobiology
  - Reliable estimates of uncertainty

- Development of biomarkers of radiation susceptibility and postflight risks

- Initiation of developmental radiobiology research

- Breakthroughs in radiobiological studies

6.6.3 Phase 3, 2010–2023

- Radiation risk predictions for early and late radiation effects
  - Accurate to ±50 percent
  - Validated in space

- Synergies of radiation risk with hypogravity understood and included in risk predictions

6.7 Enable Human Presence in Space

6.7.1 Phase 1, 1998–2002

- International agreements on radiation dosimetry in space implemented
  - Instrument intercalibrations complete

- Ethical issues resolved: acceptable risk, astronaut selection, ALARA, postflight medical surveillance, and so on

- Tours of duty/mission length required to stay within career radiation limits defined for LEO

- Flight rules implemented for the ISS to stay within yearly radiation limits

- Flight rules implemented for EVA

- Radiation forecasting, warning, and monitoring implemented for the ISS

- Emergency medical responses defined for unplanned radiation exposures (for example, SPE)

6.7.2 Phase 2, 2003–2009

- Design of exploration spacecraft to maintain crew radiation exposures within radiation limits

- Design of planetary surface habitats to keep human radiation exposure within radiation limits for 5-year stay on Mars
  - Optimization of planetary surface shielding

- Radiation forecasting, warning, and monitoring implemented for deep space travel

- Emergency medical responses defined for unplanned radiation exposures (for example, SPE)

- Countermeasures for proton radiation (for example, radioprotectants)

- Operational strategies implemented for deep space missions ALARA

6.7.3 Phase 3, 2010–2023

- Design of planetary surface habitats to keep human radiation exposure within radiation limits for permanent planetary surface colony
  - Optimization of planetary surface shielding

- Radiation forecasting, warning, and monitoring implemented for planetary surface colony

- Emergency medical responses defined for unplanned radiation exposures (for example, SPE)

- Countermeasures based on molecular biology mechanisms for prevention and postexposure intervention to mitigate HZE radiation injury

- Operational strategies implemented for planetary surface ALARA

DELIVERABLES

7. Management Strategy

7.1 Activities

The following activities are part of this Space Radiation Health Program.

7.1.1 Basic Research

- The development of research needs (advisory committees, NCRP, NAS/NRC, and so on)

- An investigator-initiated research program

- Peer review and selection

- Grant and contract management

- Workshops and symposia

- Participation in scientific and technical meetings

- NSCORT

7.1.2 Advanced Technology Development

- Instrumentation and dosimetry

- Telescience and robotic radiobiology

7.1.3 Coordination With Other NASA Activities

- The NASA Enterprises

- The ISS

- Exploration planning

- The NASA Field Centers

- The National Space Biomedical Research Institute (NSBRI)

7.1.4 Coordination With Other Federal Agencies and Private Institutions

- The use of Loma Linda facilities

- The use and operation of AGS

- The construction and operation of BAF

- The NASA Field Centers

- NSBRI

7.1.5 Coordination With International Partners

- Coordination of Space Station dosimetry

- Space Station radiation science and validation

- Workshops and symposia

- Personnel exchanges (students, postdoctoral fellows, scientists)

7.1.6 Implementation

- Implementation Plan

- Validation of ground-based predictions

- The development and implementation of flight rules

- Definition of roles and responsibilities

7.1.7 Outreach

- Web page with program information

- Brochures, posters, and conference displays

- Responses to public requests for information

- A list of speakers

7.2 Assets and Resources

7.2.1 NASA Headquarters

Code U

- Space Radiation Health Program

- Materials Science Program

- Shuttle/*Mir*

- The ISS

- Mars 2001

Code S

- Ongoing and planned missions for data on space environment (ACE, SOHO, and so on)

- Solar physics for forecasting

Code M

- Space Environment Effects at Marshall Space Flight Center

- Exploration planning

Headquarters Radiation Coordinating Team

- Codes UL (lead), UG, S, R, M, and A

7.2.2 NASA Centers

Marshall Space Flight Center

- Environment definition (Space Science Lab)

- Materials testing (Materials Lab)

- EEE parts (Astrionics Lab)

- System effects modeling (Systems Lab)

- SEE Program Management (Systems Lab)

Johnson Space Center

- Radiation health

- Radiation dosimetry

- Space radiation environment studies

Jet Propulsion Laboratory

- Robotic precursor missions

- Space science

- Space radiation environment studies

Langley Research Center

- Shield materials and radiation transport

- Mission and shield analysis

- Systems concepts and analysis

Figure 4. Roles and Responsibilities: Organization Chart
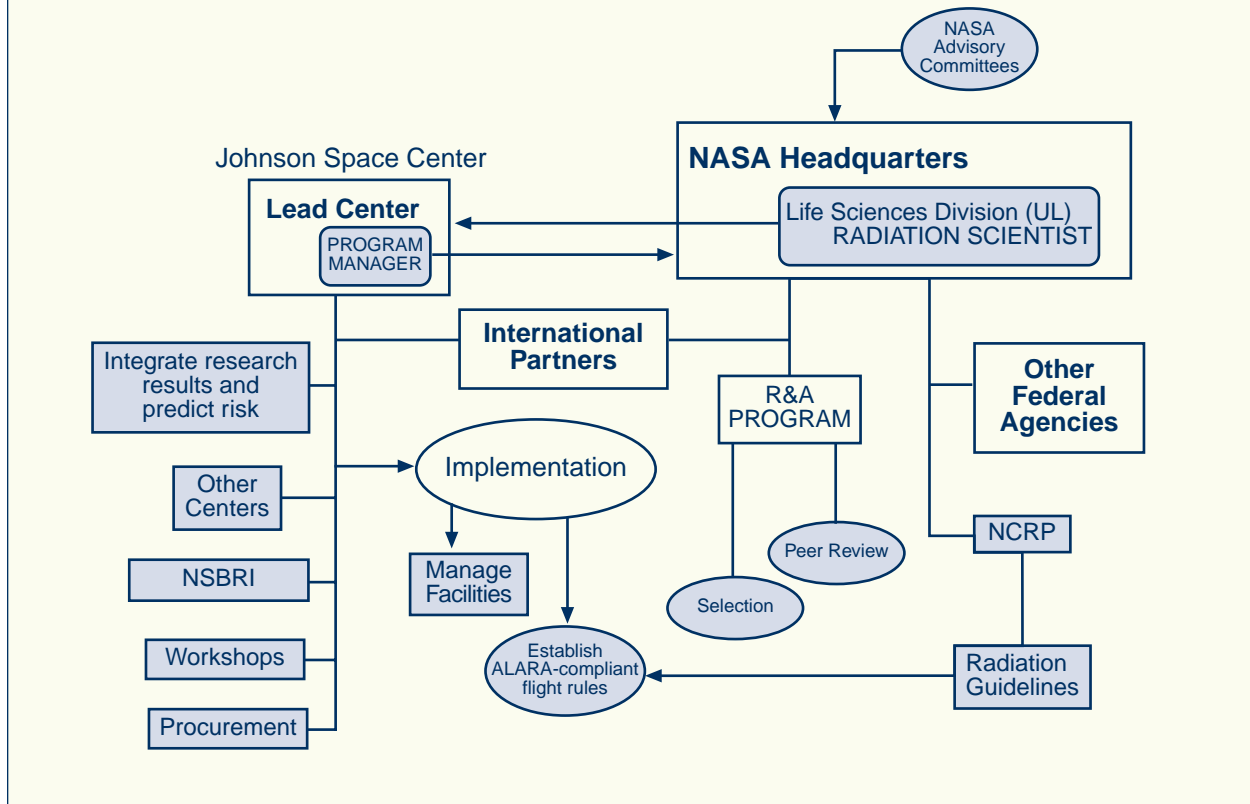
7.3 Roles and Responsibilities

This section describes the roles and responsibilities of the participants in the program. A schematic chart describing these roles is shown in Figure 4.

7.3.1 NASA Headquarters

Advisory Committees

• Aerospace Medical Advisory Committee

• Life Sciences Advisory Subcommittee of the Life Sciences and Applications Advisory Committee

Consulting Groups

• NAS/NRC

• National Council of Radiation Protection and Measurements

• NASA/National Institutes of Health Advisory Committee on Biomedical and Behavioral Research

Customer Input

• Radiation Coordination Team (NASA Headquarters)

• Science Advisory Committee on Radiobiology (BNL)

• Science Advisory Committee for Proton Research (Loma Linda University)

MANAGEMENT STRATEGY

7.3.2 Life Sciences Division

- Represents the NASA Space Radiation Health Program

- Coordinates NASA radiation activities

- Develops, solicits, reviews, and selects basic research grants and contracts

> **Peer Review**
>
> All research and development activities conducted with NASA Space Radiation Health sponsorship shall be peer reviewed by independent, external peer review panels adhering to the same standards as all other science programs in the Life Sciences Division.

- Interacts with international partners, other Federal agencies, universities, and other research institutions

- Provides NSCORT oversight and supervision

- Interacts with NCRP, NAS, and NASA advisory groups

- Approves budgets and schedules

- Approves the Implementation Plan

7.3.3 Johnson Space Center

- Supports NASA Headquarters development of the strategic plan/roadmap

- Develops and executes the Implementation Plan with integrated schedules, milestones, and deliverables

- Develops budgets, and procures and manages selected contracts and grants

- Leads independent analyses and assessments, and develops tools to integrate emerging data into models useful for mission design

- Collaborates with NSBRI

- Organizes and conducts workshops

- Coordinates the development, review, and implementation of flight rules related to radiation exposure under ALARA

- Works with implementing Field Centers to integrate reports and catalog data, including ensuring the preparation of a Radiation Protection Handbook

- Supports outreach

7.3.4 Langley Research Center

- Leads the development of radiation transport tools and the optimization of shielding materials

- Coordinates radiation and aeronautics (AIR program)

7.4 Metrics

- Hours of beam time *requested* at ground-based facilities

- Hours of beam time *used* at ground-based facilities

- Papers published in peer-reviewed journals

MANAGEMENT STRATEGY

- Patents obtained

- The number of proposals responding to solicitations/the number of proposals accepted (flight and ground)

- Estimated reduction in risk uncertainties

- Radiation dose prediction—accurate prediction of radiation dose on the Shuttle, *Mir*, the ISS, and exploration missions

- Radiation shielding—improvement in radiation shielding from the Shuttle and Station levels by a factor of X

- Radiation risk prediction—improvement in the prediction of health risks from space radiation exposure so that the accuracy of risk estimates is comparable to that for terrestrial illnesses

- SPE prediction and monitoring—accurate prediction and warning to crew of increased energetic proton flux with to be determined hours' warning time and no more than to be determined percentage of false alarms

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Task Books

To facilitate a better understanding of the research NASA supports, the NASA Office of Life and Microgravity Sciences and Applications (OLMSA) has developed comprehensive annual publications, called task books. These task books, one for each division, include descriptions of all peer-reviewed projects, or tasks, funded by the Life Sciences and Microgravity Science Divisions during all or part of a particular fiscal year. Investigators are required to update respective task book entries on an annual basis. The information for each task consists primarily of a task

description, task progress, and a list of publications, presentations, and other accomplishments (such as journal articles, books and book chapters, published meeting papers and abstracts, NASA technical documents, and patents) for that fiscal year.

Task books from 1995 onward are available online at the following World Wide Web address: *http://peer1.idi.usra.edu/peer_review/taskbook/taskbook.html*

The Space Radiation Health Program, together with several useful links, is described online at: *http://www.hq.nasa.gov/office/olmsa/lifesci/spacerad.htm*

NASA-related activities at the Brookhaven National Laboratory are described at: *http://bnlstb.bio.bnl.gov/www_root/webdocs/nasa/nasapage.htmlx*

NASA-related activities at Loma Linda University are described at: *http://www.llu.edu/llu/ci/nasa/*

Workshops and Working Groups

A number of workshops and working groups have been sponsored by the Space Radiation Health Program to better define programmatic goals and

directions. A limited number of proceedings of these workshops are available.

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The following is a summary of some of the more salient conclusions regarding the space radiation problem, since 1961:

• Space Science Board, National Research Council, "First Summary Report," 1961

• Space Science Board, National Research Council, "Radiobiological Factors in Manned Space Flight," 1967

• Radiobiological Advisory Panel, Committee on Space Medicine, Space Science Board, "Radiation Protection Guides and Constraints for Space-Mission and Vehicle Design Studies Involving Nuclear Systems," 1970
  – Recommended career limit for whole body exposure: 4 Sievert (Sv) (based on leukemia risk)
  – Additional limits: skin (12 Sv); testes (2 Sv); lens of eye (6 Sv)
  "Present knowledge . . . does not permit establishment of dose-effect relationship to the degree of accuracy desired for spacecraft design and operational planning."

• Grahn, D., (ed.), National Academy of Sciences, "HZE Particle Effects in Manned Spaceflight," 1973
  – Experimental data available are inadequate; detailed physics and biology studies are essential.
  ". . . a quantitative assessment of the potential hazard [of HZE particles] should be in hand before . . . missions are carried out beyond the earth's magnetosphere or in high-inclination earth orbit."
  – Ground-based facility is essential.
  "We recommend most strongly that at least one accelerator be modified to be capable of accelerating particles of atomic numbers up to . . . iron, and preferably higher, with energies of at least 500 MeV/nucleon. Such accelerators . . . must have closely associated facilities to provide support for advanced biological and medical research."

• National Council of Radiation Protection and Measurements, "Guidance on Radiation Received in Space Activities," NCRP Report No. 981989
  – Limited to LEO
  – Recommended career limits for whole body exposure based on lifetime excess risk of cancer mortality of 3 percent/Sv (1–4 Sv depending on gender and age)
  – Limits for deterministic effects: skin (6 Sv); lens of the eye (4 Sv)
  – Currently under revision

• NASA Aerospace Safety Advisory Panel, "Annual Report," Finding #14, 1997

"Extended deployment by astronauts in [the] ISS could result in radiation exposures that exceed those [i.e., DOE Radiation Worker] limits. Radiation exposure is cumulative over a lifetime. Design features of the ISS to minimize crew exposure to ionizing radiation are unknown. The dangers of exposure to ionizing radiation should be confronted now with conservative module, system, and equipment designs that minimize exposure. Otherwise, crew stay time may have to be limited."

A meeting to develop a NASA-wide, crosscutting strategic approach to radiation issues was held at Langley Research Center on September 29, 1996. The meeting was attended by Headquarters personnel and Field Center representatives. The following consensus recommendations were made:

1. A NASA-wide, interdisciplinary task force should be assembled to coordinate all Agency radiation-related activities.

2. The availability of a facility to simulate the HZE part of the space radiation spectrum was considered to be mission critical for progress in dealing with space radiation problems.

3. A single Lead Center for management of the evolving programmatic activities would not be appropriate because the focus of such activities would be expected to change as progress was made.

4. Efforts to develop the required knowledge were timely: NASA has suffered from not making the necessary investments in the past; the results obtained from research and development in space radiation are permanent and would remain current and useful even if exploration milestones are delayed.

Subsequently, the Associate Administrator of OLMSA directed that a plan be developed according to the following principles:

1. Involve the Lead Center (Johnson Space Center) in developing this plan, including input by spacecraft designers

2. Consider nontraditional approaches for leveraging ongoing research activities from other U.S. agencies, programs within the HEDS Enterprise, and international partners

3. Address issues of age and gender and applicability of nonhuman studies in establishing occupational limits and risks to humans (relevance and extrapolation accuracy)

4. Identify methodology by which results from different prospective studies will be translated into spacecraft design and/or policies and procedure

APPENDIX A
ADDITIONAL BACKGROUND

5. Establish mechanisms by which methodologies in item 4 above can be validated to minimize errors that impact costs or schedules

6. Develop an integrated schedule and budget profile taking into consideration all the relevant contributions made by other agencies and programs within NASA

7. Consider alternative and innovative ways to gather the information

Appendix B
Radiation Limits

Radiation Limits for Low–Earth Orbit (LEO)

In 1989, the National Council on Radiation Protection and Measurements (NCRP) issued Report No. 98, "Guidance on Radiation Received in Space Activities," recommending the new limits for radiation exposure in low-Earth orbit (LEO), as shown in Table II. On December 14, 1989, the NASA Administrator, Admiral Richard H. Truly, notified the Occupational Safety and Health Administration (OSHA) of formal acceptance of these recommendations by NASA. A copy of his letter, summarizing the existing situation, is shown in Figure B.1(a). As noted in Admiral Truly's letter to the Assistant Secretary for OSHA, all Federal agencies are under OSHA regulations by Executive Order 12196 of February 26, 1980, and all NASA Earth-based activities conform to applicable OSHA regulations. However, such standards have been adjudged by OSHA to be inapplicable to space activities, and NASA was advised of the need to devise and adopt supplementary standards to govern radiation risk management of its space activities.

In 1981, standards recommended by the National Research Council of the National Academy of Sciences (NAS/NRC) were accepted as the supplementary standards by the Secretary of Labor. Based on new

Table II. Dose Limits for STS and ISS
NCRP Report 98 (1989)[a, b]

	BFO[c] (5 cm)	Eye (0.3 cm)	Skin (0.01 cm)
30-Day	0.25	1.0	1.5
Annual	0.5	2.0	3.0
Career[d]	1.0–4.0	4.0	6.0

[a] Units are 1 Sievert (Sv) = 100 rem at the depth indicated in parentheses.

[b] These limits do not apply to missions outside LEO.

[c] BFO = blood-forming organs.

[d] The career limits depend on gender and on age at beginning of exposure, according to:

$$2.0 + 0.075 \times \begin{cases} (\text{age} - 30) \text{ for males} \\ \text{and} \\ (\text{age} - 38) \text{ for females} \end{cases}$$

Figure B.1. Correspondence Establishing Current NASA Radiation Limits

(a)

(b)

information gained since 1970, NASA subsequently requested the NCRP to reevaluate these standards, leading to the recommendations shown in Table II, which currently govern radiation exposure in LEO. These radiation standards were approved by OSHA in March 1990; a copy of the letter from the OSHA Administrator to the NASA Administrator is shown in Figure B.1(b). No limits are currently set for exploration class missions, although specifications for the required data base are being developed by the NCRP.

The LEO limits are based on treating the radiation exposures of crew members and payload specialists as an occupational hazard and to evaluate their risks in terms of those to radiation workers and to workers in other industries. On this basis, the NCRP concluded that the recommended career limits for astronauts should be based on a lifetime absolute excess risk of cancer mortality, caused by cancer, of 3 percent. In other words, the risk of cancer mortality incurred by humans in space should be no more than 3 percent greater than the cancer risk suffered by the general worker population that is not exposed to space radiation. This consideration defines the career limits; the 30-day and annual limits restrict radiation exposure to remain below the threshold for short-term radiation effects.

The development of radiation standards in space has followed a different path than that of radiation standards on the ground. Radiation protection standards for workers in radiation-related occupations and for the public inadvertently exposed to artificial, or human-made, sources are shown in Table III. They are based on common sense principles of avoiding exposure to the extent possible, ensuring that exposures do not exceed threshold levels for acute biological effects, and limiting the risk of delayed effects (such as cancer or genetic effects) to reasonable values.

The NCRP is currently revising the radiation limits recommended for LEO and, hence, for the ISS, taking into account new data and new concepts of acceptability of risk. Draft limits, assuming acceptability continues to be set at the level of 3-percent excess lethal cancer risk, are shown in comparison with existing career limits in Figure B.2. The proposed new career limits are significantly lower than the current career limits. The acceptability criterion of 3-percent excess cancer risk was based on data on excess lethality associated with various common occupations, using that for "medium safe" occupations as the accepted criterion. In the meanwhile, as U.S. industry has become safer, lower levels of excess cancer risk may become the standard of acceptability.

Table III. Dose Limits on Earth
ICRP Publication 60 (1990)

**Occupational Exposure
(monitored radiation workers)**

Whole Body	Sv
Max. Yearly Effect Dose	0.050
Max. Effective Dose in 5 Years	0.100

Other (max. yearly equivalent dose)

Lens of the eye	0.150
Skin	0.500
Hands and feet	0.500

General Public

Whole Body	Sv
Max. Yearly Effect Dose	0.001

Other (max. yearly equivalent dose)

|	
Lens of the eye	0.015
Skin	0.050
Hands and feet	—

APPENDIX B
RADIATION LIMITS

ALARA

Radiation limits are regarded as an upper limit of acceptability, and the principle called ALARA (as low as reasonably achievable) is intended to ensure that most exposures will be well below the limit. Adherence to this principle has been adopted by NASA and is part of the rationale used for arriving at the supplementary standards for space, which also included the following considerations:

Figure B.2. Draft NCRP Limits for the ISS

- The population involved in space activities is of limited size; thus, genetic effects would not play a role.

- The benefit of space flight exceeds substantially the risk incurred by increased exposure to radiation.

- A formal appraisal of radiation hazards would be conducted before each mission to incorporate a proper limitation of radiation risk into each mission's design.

- Actual radiation exposure of crew members would be monitored by individual and area dosimeters, and records of all radiation exposures for every crew member would be maintained (including those from medical procedures).

- Formal protocols, including the use of calibrated active and passive measurement radiation systems, and flight rules covering any radiation exposure contingency have been developed and documented.

Radiation Limits Beyond LEO

Already in its Report 98, the NCRP pointed out that the knowledge of radiation risk, available from conventional (sparsely ionizing, low linear energy transfer or low-LET) radiation such as x-rays or gamma rays, is inadequate for the assessment of radiation risk in space. The physics and biology of space radiation are poorly known, if at all. In addition, space radiation results in new and qualitatively different biological effects, either not seen or not seen at comparable radiation levels for low-LET radiation.

Methods to manage radiation risks in space are insufficient. Avoidance strategies require forecasting and warning capabilities that are not available. Shielding optimization requires knowledge of nuclear interactions and biological characterization of radiation fields inside materials and tissues, which is sparse when it is available at all. Pharmaceutical, chemical, or molecular prevention and intervention methods are not available for space radiation. In conclusion, current knowledge of radiation effects in space is not adequate for the design of long-duration missions without incurring either unacceptable risks or excessive costs.
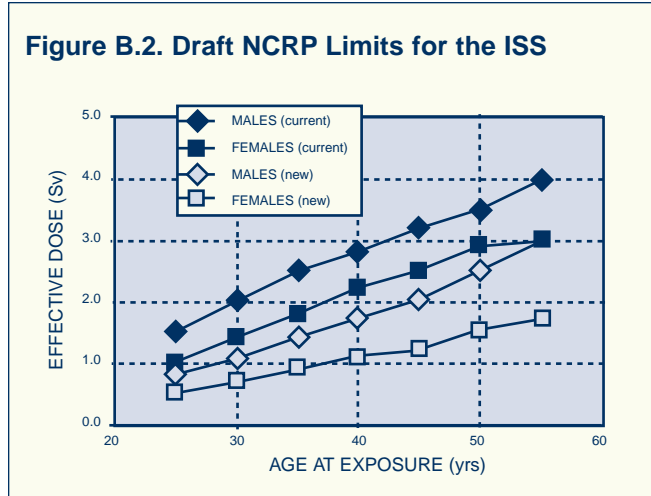
An awareness of this problem has existed at least since 1961, when the Space Science Board of the NRC published its "First Summary Report." This was followed by a report on "Radiobiological Factors in Manned Space Flight" in 1967. In 1970, the Radiobiological Advisory Panel of the Committee on Space Medicine of the Space Science Board recommended a career limit for whole body exposure of 4 Sievert (Sv), based on leukemia risk, in the report titled "Radiation Protection Guides and Constraints for Space-Mission and Vehicle Design Studies Involving Nuclear Systems." Additional limits were set for skin (12 Sv), testes (2 Sv), and lens of eye (6 Sv). In its report, the panel concluded: "Present knowledge . . . does not permit establishment of dose-effect relationship to the degree of accuracy desired for spacecraft design and operational planning."

For the past 36 years, every learned body that has examined this problem has arrived at similar conclusions: radiation risks must be understood on the basis of experiments conducted at ground-based laboratories where adequate simulation of space radiation is possible. Space-based experimentation is required only in those cases in which essential data are not accessible on the ground, to validate model predictions, and to examine the interaction of radiation and hypogravity. Progress was made as long as major radiation research programs and accelerator facilities were supported by the Department of Energy, the Department of Defense, the National Cancer Institute, and other groups with an interest in radiation hazards. This is no longer the case, and NASA must assume a much larger share of responsibility for developing the required data base and using it to predict risk from radiation exposure in space.

In the most recent analysis of the NASA radiation problem, the Task Group on Biological Effects of Space Radiation of the National Academy of Sciences (NAS) concluded that there are seven high-priority research questions that need to be addressed. These are:

- What are the carcinogenic risks of protons and heavy-ion energetic (HZE) particles?

- How do cell killing and chromosome aberrations vary with shielding composition and thickness?

- What can be done to increase confidence of extrapolation from mouse data to humans?

- What are the risks to the central nervous system from HZE?

- How can better error analyses be performed?

- How do the design and materials of vehicles affect the radiation environment?

- Can solar particle events be predicted with sufficient warning?

The NAS task group also listed five additional questions of lower priority related to (1) fertility, (2) cataracts, (3) drugs to reduce effects, (4) assays for susceptibilities, and (5) variations of response for different par-

ticles of the same LET. The questions identified by the NAS task group are not substantially different from the critical questions developed by the Aerospace Medicine Advisory Committee of the NASA Advisory Council in June 1992, which are listed in Appendix H.

For those priorities requiring ground-based accelerator beams, the NAS task group estimated both the least amount of beam time required (about 3,000 hours) and the duration of such research if (1) 100 hours per year of HZE beam-time were available or (2) 2 weeks per year of beam time were available or (3) 3 months per year of time were available. They assumed that the number of biological endpoints, particle types, and energies were kept to a minimum. They concluded that the first and second scenarios would require more than 20 years to carry out the necessary research. However, the third scenario of 3 months per year of beam time might reduce the accelerator work to as little as 10 years. The NAS task group recommended that NASA should explore various possibilities to increase the research beam time available for experiments with HZE particles, including the use of accelerators other than the AGS accelerator at BNL and the construction of new facilities.

In the weightless or subgravitational environment of space, humans experience a multitude of physiological and psychological effects. The interactions of these effects with the biological effects caused by radiation are not known. The uncertainties associated with predicting radiation risk are very large, even on the ground.

The usual approach to risk prediction, implicit in the NCRP calculation of radiation limits, is illustrated in Figure C.1. The available information consists, among other data, of observed frequencies of cancer in different tissues of A-bomb survivors, calculated **doses**, and estimates of neutron energies at the location of exposure for each survivor (the extent to which neutrons are a significant contribution is still somewhat controversial).

The doses are multiplied by a **quality factor** derived from estimates generated by one or more international bodies, such as the International Council of Radiation Protection and Measurements (ICRP). This product is denoted as **dose equivalent**, in units of Sv. The frequency of lethal cancer for A-bomb survivors, as a function of dose or dose equivalent, is then extrapolated to zero dose, and the initial slope of the curve yields the increase in probability per unit dose equivalent. However, occupational exposures, especially in space, take place at very low radiation intensities, and the accumulated dose is much lower than that suffered by the majority of A-bomb survivors. A **dose and dose rate effectiveness factor (DDREF)** is used to take this difference into account. It reflects the fact that cells and tissues can repair small incremental damage caused by radiation at low doses and dose rates associated with occupational exposure. This is in contrast with the high dose rate and generally high doses delivered to the A-bomb survivors.

The normal lifetime expectation of cancer death for the U.S. population is approximately 20 percent. Current consensus (as discussed, for example, in the CIRRPC report) is that the probability of lethal can-

Figure C.1. Current Model for HZE Risk Prediction
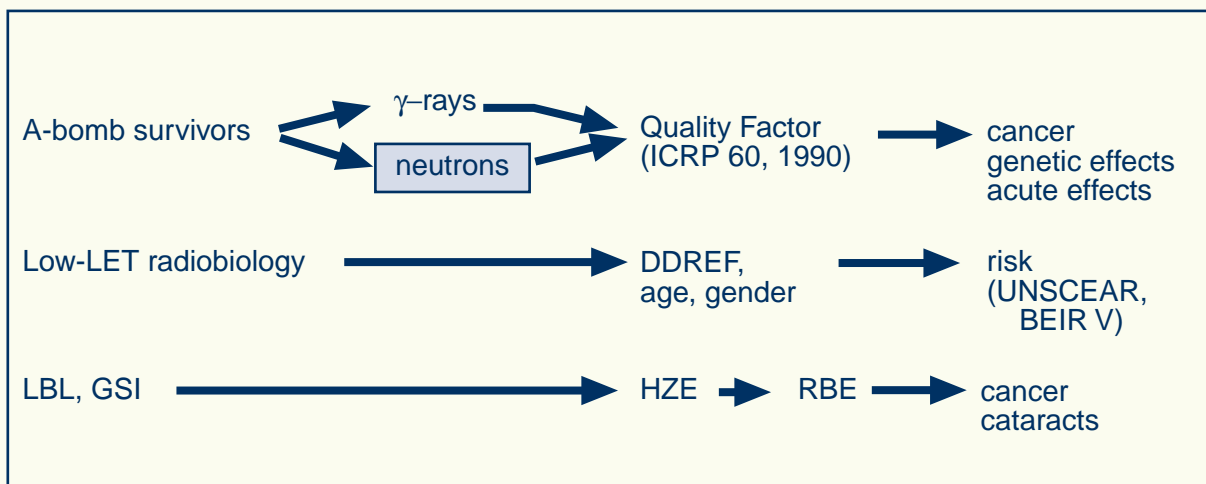
cer from occupational exposure to low-LET radiation increases by approximately 4.5 percent per Sv for the general population and 3.5 percent for the working-age population (individuals between the ages of 18 to 65). The difference arises because the general population includes children and other vulnerable individuals, whereas the working population is restricted to adults. These estimates are considered valid for dose equivalent less than approximately 0.1 Sv and low dose-rate exposure. According to the CIRRPC report, the uncertainty associated with this estimate is a factor of 2—that is, at low doses and dose rates, the increase in lethal cancer risk may be as little as 1.7 percent or as much as 7 percent per Sv, for the working population, at the reference level of 0.1 Sv. This report also concludes that data ". . . on exposed human populations contribute little to scientific understanding of lifetime total cancer mortality at absorbed doses below about 0.2 to 0.5 Gy." (The reference for this conclusion is an article by Shimizu, Y., Kato, H. and Schull, W.J. "Studies of the Mortality of A-bomb Survivors: 9. Mortality, 1950–1985: Part 2. Cancer Mortality Based on the Recently Revised Doses" (DS86), *Radiation Research* 121: 120 (1990).)
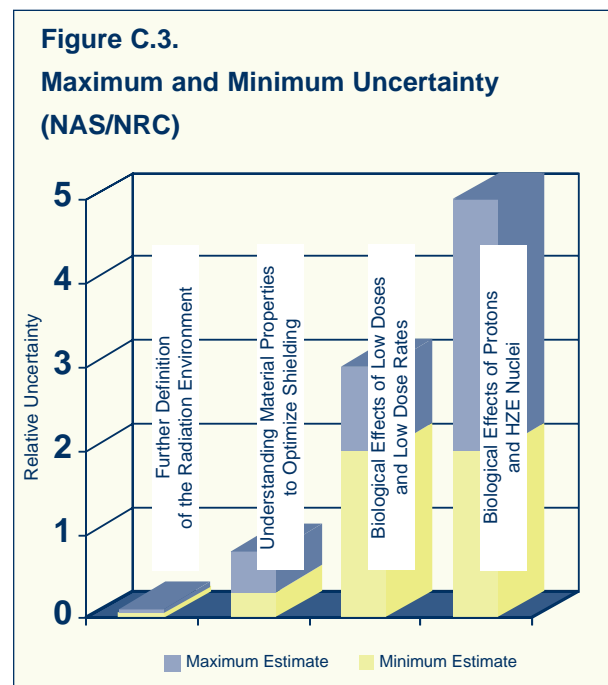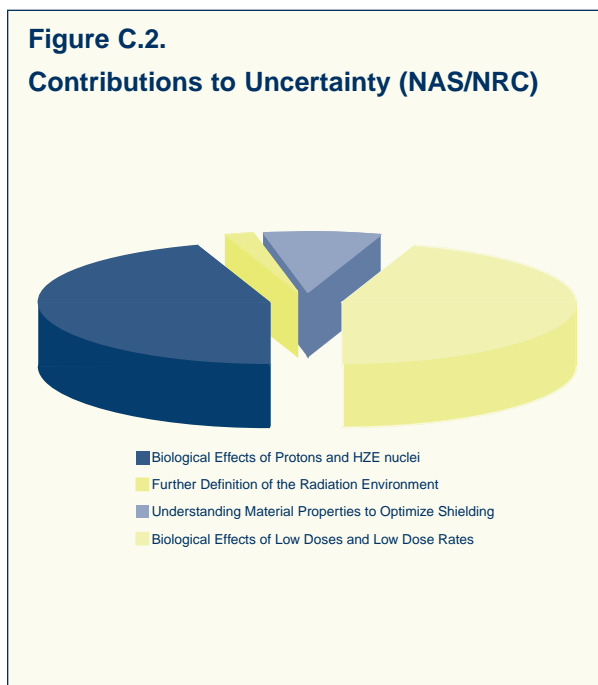
Finally, the sparse available data obtained from laboratories such as the Lawrence Berkeley Laboratory or the heavy ion research institute (GSI) in Darmstadt, Germany, are used to guide modifications attributed to the fact that the very large ionization density of HZE particles results in a range of measured values of **relative biological effectiveness (RBE)** that depend on the **linear energy transfer (LET).**

According to this model, there are four sources of correlated uncertainty that need to be considered in estimating the accuracy of risk predictions:

- The uncertainty in the prediction of the number, kind, and energy of particles predicted to be present in the space radiation environment

- The uncertainty in the number, kind, and energy of particles predicted to be present inside any shielded space environment (spacecraft, the ISS, planetary surface, and so on) and inside the tissues of crew members

- The uncertainty in the relationship between risk endpoint (for example, excess cancer) and the calculated dose equivalent in the space environment, because of the coarseness of DDREF estimates

- The uncertainty in the quality factor from the different LET of the HZE particles, which leads to significantly different biological effects for equal doses of different particles

The NAS/NRC report estimates that the overall uncertainty in predicting the additional cancer risk induced by exposure to space radiation is from 4 to 15 times larger or from 4 to 15 times smaller than calculated according to the best currently available data and methods. The biological factors account for the bulk of this uncertainty, and their uncertainty acts to amplify the smaller uncertainties in the physical environment and the shielded environment. The uncertainties estimated by NAS/NRC are shown in Figure C.2 and Figure C.3. These uncertainties result in substantial penalties for missions and mission designs, such as:

- On the ISS, uncertainties in risk estimation combine with ALARA to constrain the length of tours of duty. Exchange of crew members is expensive. If a more accurate risk prediction would warrant fewer crew exchange missions, substantial savings could be accrued.

- Shielding required by conservative designs may result in excessive weight and cost for a given exploration design architecture or severely constrain the range and pace of manned planetary surface exploration.

- Underestimates of accrued radiation risk may result in unacceptable performance deficiencies or long-term health problems for crew members returning otherwise safely from an extended mission.

Figure C.2.
Contributions to Uncertainty (NAS/NRC)

■ Biological Effects of Protons and HZE nuclei
■ Further Definition of the Radiation Environment
■ Understanding Material Properties to Optimize Shielding
■ Biological Effects of Low Doses and Low Dose Rates

Figure C.3.
Maximum and Minimum Uncertainty (NAS/NRC)

Relative Uncertainty

Further Definition of the Radiation Environment

Understanding Material Properties to Optimize Shielding

Biological Effects of Low Doses and Low Dose Rates

Biological Effects of Protons and HZE Nuclei

■ Maximum Estimate   ■ Minimum Estimate

The above considerations translate into a compelling need to reduce the existing uncertainties in space radiation risk predictions as the key to solving the "radiation problem" in space.
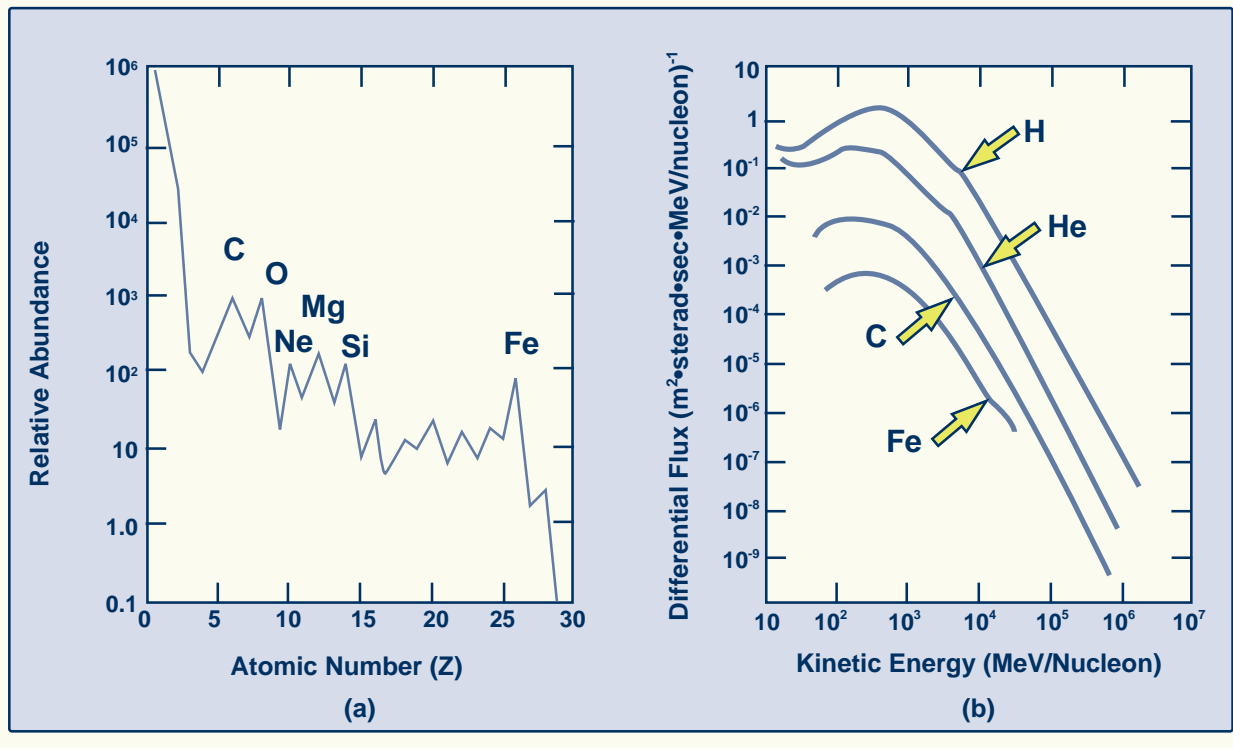
The components of space radiation that are of concern are the high-energy, charged nuclei of elements from hydrogen (protons) to iron (high-energy nuclei with charges greater than 2 are also referred to as **HZE particles**). These particles are part of the **galactic cosmic ray (GCR) background** radiation that permeates interplanetary space. As shown in Figure D.1(a), the fraction of GCR constituted by the nuclei of elements heavier than helium is very small; approximately, GCR consist of 85 percent protons, 14 percent helium, and 1 percent heavier particles. As seen in Figure D.1(b), showing the distribution in energy of several important HZE nuclei, these particles have very high energies, sufficient to penetrate many centimeters of tissue or other materials. In addition, the HZE nuclei are highly charged and, therefore, very densely ionizing. As a consequence, even though the number of HZE particles is relatively small, they have a significant biological impact that is comparable to that of protons.

Solar disturbances occasionally cause much larger fluxes of particles, mainly high energy protons; these are known as solar particle events (SPE). Peak flux during an SPE may be two to five orders of magnitude greater than background, within hours of the event onset, as shown in Figure D.2. Periods of enhanced flux may last for days, with successive peaks caused by multiple events and enhancements during shock passage. The energy spectra of these events vary from event to event (Figure D.3), indicating that different

**Figure D.1. Abundances (a) and Energy Spectra (b) of GCR**

physical processes are involved. However, the number of protons with energies in the region of several hundred MeV is significant in all cases.
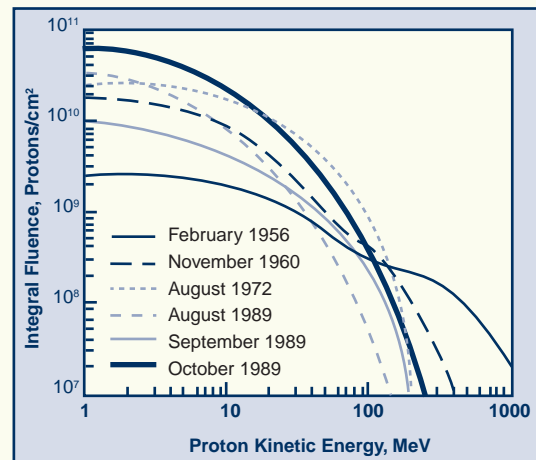
An illustration of the contribution of different components of space radiation outside Earth's magnetic field is shown in Figure D.4. This figure shows the calculated relative contribution of different groups of particles to the **dose equivalent** (refer to Appendix B for the definition of quantities) behind 3 g/cm^2 of aluminum (slightly more than 1-cm thickness). The lefthand side shows that protons account for almost all of the SPE radiation, and the righthand side shows that this is no longer true for GCR, where HZE particles account for most of the radiation risk.

Protons and electrons of sufficiently low energy can be captured by Earth's magnetic field, schematically indicated in Figure D.5, as an equivalent bar magnet. In reality, the magnetic field is more complicated. Its
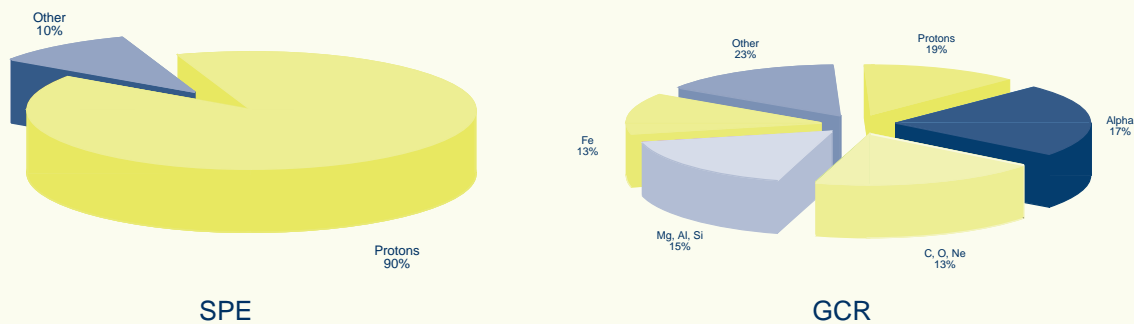
Figure D.2. Time Course of a Solar Particle Event
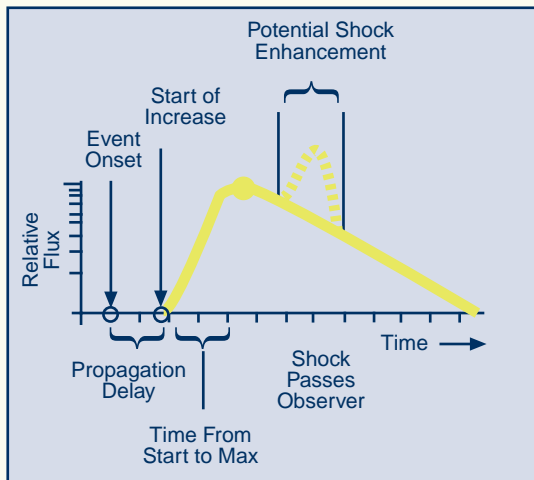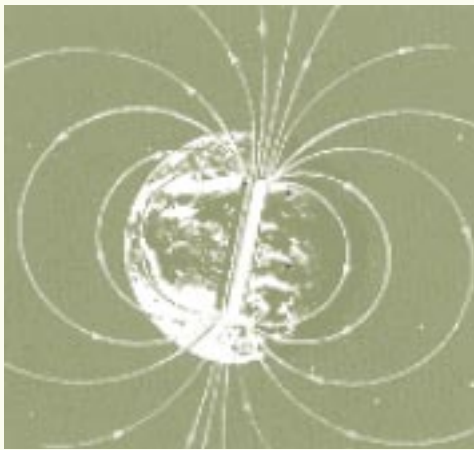

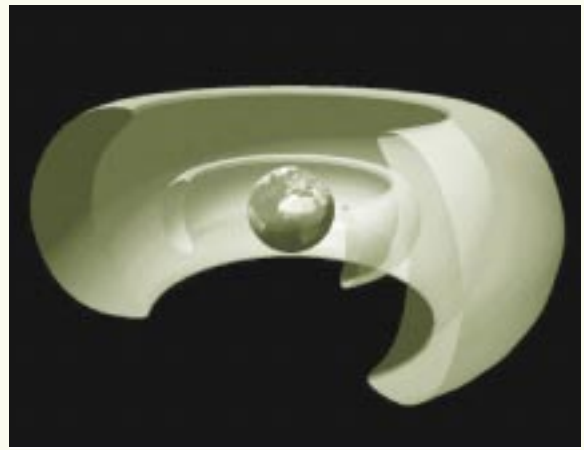**Figure D.3. Distribution in Energy of Proton Fluxes for Major Past SPE's (Free Space)**

Figure D.4. Relative Contribution of Different Components of Space Radiation to Dose Equivalent

SPE

GCR

APPENDIX D
THE SPACE RADIATION ENVIRONMENT

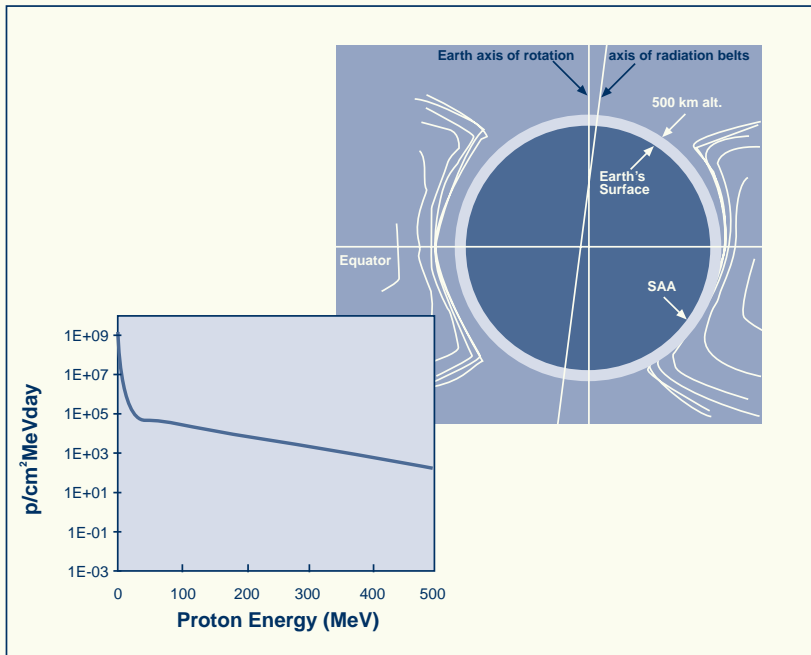**Figure D.5. Earth as a Magnet Showing Field Lines**

Figure D.6. The Van Allen Belts

shape is also distorted by the Sun so that the magnetic field on the day side is compressed and the magnetic field on the night side is pushed away. Charged particles entering Earth's magnetic field from space are turned from their path as they traverse the magnetic field lines. If their energy is sufficiently low, they are trapped into the **Van Allen belts** (Figure D.6). These trapped radiation belts surround Earth at altitudes that depend on Earth's magnetic field. The belts consist of protons (inner belt) and electrons (inner and outer belt), spiraling along magnetic field lines from pole to pole. Near the poles, the trapped radiation belts extend almost down to the surface.

Earth's magnetic field is offset and tilted from Earth's axis of rotation. Thus, the radiation belts, centered on the magnetic field, are also not centered on Earth's axis of rotation. The region where the radiation belts are closest to Earth's surface, near the coast of Brazil, is called the **South Atlantic Anomaly,** schematically shown in the inset of Figure D.7. The trapped radiation belts are not static; their altitude distribution and intensity greatly depend on solar activity, with hourly, daily, and

Figure D.7. Energy Distribution of Trapped Protons and South Atlantic Anomaly

seasonal changes. Over geological times, the magnetic field of Earth has been known to change and reverse itself. The measured long-term drift in the position of the South Atlantic Anomaly provides continuing evidence of active Earth magnetism. As shown in Figure D.7, proton fluxes at energies of hundreds of MeV, as measured on the *Mir* space station during solar minimum, can still be significant.

The magnetic field of Earth allows only the fastest, most energetic particles to penetrate deep into the atmosphere, and the thick atmosphere provides so much material that most of the incident radiation interacts before it can reach the surface of Earth. Thus, space radiation is the source of many of the cosmogenic nuclides, such as ^{14}C. At the surface of the Earth, only the most energetic, lightest products of the nuclear interactions of GCR with the atmosphere, mainly μ-mesons, are still present. This is the radiation background present everywhere on Earth.

Higher in the atmosphere, at altitudes used by commercial aircraft, radiation is more intense, and the most hazardous secondary radiation is high-energy neutrons emitted by GCR interactions with the atmosphere. The intensity of the radiation increases with altitude. At high altitude, large fluxes of high-energy protons from an SPE can cause radiation levels to exceed those permissible for aircraft passengers or crew. For this reason, radiation levels on high-altitude aircraft must be monitored, and the aircraft may be required to descend to safer altitudes during an SPE.

The Space Shuttle and ISS will be located in low-Earth orbit (LEO), beyond the protection of the atmosphere but still within the protection of the magnetic field. In these orbits, the radiation risk will be caused by GCR particles too energetic to be significantly deflected by the magnetic field, as well as by trapped radiation belt protons. When the orbit of a spacecraft intersects the South Atlantic Anomaly, radiation intensity can increase by an order of magnitude. For this reason, extravehicular activity (EVA) should be avoided whenever a spacecraft is about to traverse the South Atlantic Anomaly. Even in the interior of a spacecraft, exposures could exceed radiation limits during a large SPE. Under such circumstances, crews may be directed to limit activities to the most highly shielded area of the spacecraft for use as a "storm shelter."

Beyond Earth's magnetic field, crews are exposed directly to GCR radiation and to SPE radiation. Spacecraft or planetary habitats thus require their own measures to avoid radiation overexposures. The most fundamental measures that can be taken are to ensure that spacecraft and habitat materials are configured to provide maximum radiation shielding effectiveness, that a "storm shelter" is available, and that monitoring for SPE provides sufficient warning to crew members involved in an EVA. Other measures are possible, but they require a knowledge of biology that is not at present available.

Basic Concepts

The high-energy charged particles constituting galactic cosmic rays are nuclei of all the elements, acceler-ated to high energies, probably in supernova explosions within our galaxy. While nuclei of elements are also ejected by solar disturbances, the solar radiation of significance for radiation protection consists mainly of protons, which are the nuclei of hydrogen atoms. These nuclei are not surrounded by electrons, as would be the case for neutral atoms of elements found on Earth. They consist of Z protons and N neutrons. The chem-ical properties of an element are defined by the number of protons, Z, also known as its atomic number, and by its atomic weight. In the absence of electrons, the atomic weight is A (= N + Z), although, even in the fully neutral atom, the Z electrons surrounding the nucleus contribute only a negligible amount to the total mass.

The neutrons and protons are generically called "nucleons" to indicate that they share a major property: the response to the nuclear forces that keep the repulsion between the Z electrically charged protons from disintegrating the nucleus. A "standard nucleon," or **atomic mass unit,** is defined as the average mass per particle of a ^{12}C nucleus (containing exactly six protons and six neutrons). This corresponds to approx-imately 1.7 x 10^{-27} kg. According to Einstein's relation, $E = mc^2$ (where E is the relativistic total energy, c is the speed of light, 3 x 10^8 m/sec or 186,000 miles/sec, and m is the mass), if an atomic mass unit were entirely converted into energy, it would be equivalent to approximately 931 MeV, which is the unit in which the masses are commonly described. For comparison, the equivalent amount of energy contained in an electron mass, 0.51 MeV, is almost 2,000 smaller, with notable effect on their interaction with matter.

The high energy of these nuclei means that they are moving so fast that their velocity is measured as a fraction of the speed of light, c. The nucleons inside the nucleus all move at the same velocity because they are traveling as a group. The speeding nuclei will interact with the materials they penetrate, and they will manifest different properties depending on the type of interaction.

Interactions with atomic electrons are caused by the electrical interaction between the (negative) charge of the electrons of elements in the material and the (positive) charge of the protons in the projectile. These charges are sensed by each of the participants over large distances, in which the protons in the incident nucleus appear as a single cluster with charge Z, moving at the average velocity of the nucleons. These interactions are entirely similar to friction and cause the fast, high-energy particles to slow down. When the energy transferred to atomic electrons is large enough, one or more electrons may be removed from the atom altogether, leading to a disruption of the chemical bonds that link atoms and molecules. Evidently, when the disrupted molecules are inside a living cell, serious damage is likely to occur.

Every once in a while, the track of a nucleus penetrating through materials will come close to the nuclei of atoms in the material. When this happens, the target nuclei, the projectile nuclei, or both may break
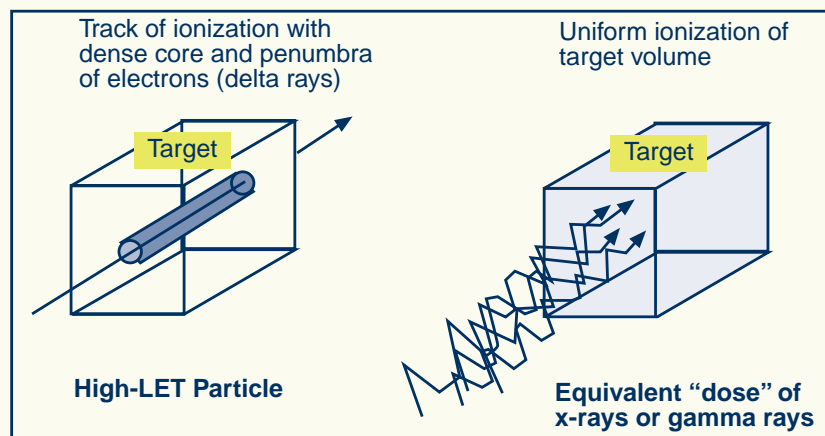
up, and energetic parts of nuclei will then fly off and continue to interact with the material. These secondary radiations may be gamma rays, neutrons, protons, nucleon clusters, or subatomic particles, such as π-mesons, created in the collision. Because these collisions occur at close quarters, the nucleus will be sensitive to the position and velocity of individual interacting nucleons from both the projectile and the target.

The energy available for each collision of nucleons will be the **energy per nucleon**, and not the kinetic energy of the whole nucleus, unless the nucleus interacts as a coherent unit. For this reason, the energy of HZE particles is commonly described in terms of energy/nucleon. For example, in an HZE nucleus consisting of A nucleons moving at 80 percent of the speed of light, the energy per nucleon is 620 MeV/nucleon, which can also be written as 620A MeV.

Energy Loss

Heavy charged particles lose energy in matter in a manner entirely different from other types of radiation. A proton or HZE particle suffers a very large number of energy losses interacting with atomic electrons in materials. Each of these losses is generally very small from the point of view of the incident particle, but may be quite large from the perspective of the electrons in the path. Especially while the particle is still going at high speed, the energy may be sufficient to detach the electron from its atom (that is, **ionize** the atom) while imparting only small deviations to the trajectory of the incident particle. The emerging electron may have sufficient energy to ionize other electrons in its turn, and a cloud of electrons of very many energies will be generated as a **track** around the particle trajectory. The pattern of energy loss of a proton or HZE particle will thus be characterized by a dense track of ionizations and atomic excitations, along a straight line corresponding to the particle trajectory. The high density of energy loss per unit path length is described as the **linear energy transfer (LET).** These facts are summarized in the left sketch of Figure E.1.

Figure E.1. HZE Particles Have a Unique Structured Pattern of Energy Deposition

Track of ionization with dense core and penumbra of electrons (delta rays)

Uniform ionization of target volume

Target

Target

High-LET Particle

Equivalent "dose" of x-rays or gamma rays

In contrast, electrons, even at high energies, are so light that most collisions with other electrons will result in a significant deviation from their path. Thus, the path of an electron in matter consists of a very large number of changes of direction. Radiation that does not consist of charged particles, such as x-rays, gamma rays, and neutrons, in general will only ionize atoms in the

material indirectly. X-ray and gamma ray photons can be absorbed by electrons and atoms to yield energetic electrons (and, sometimes, secondary photons), and neutrons generate charged particles in nuclear interactions. In either case, the probability of an energy deposition event is uniform throughout the target volume, as shown on the right side of Figure E.1.

In the case of indirectly ionizing radiation, photons or neutrons are removed from the incident number as a function of depth, with a constant probability per unit path length (described by a **cross section**) leading to an exponential pattern of energy deposition as a function of depth. In contrast, heavy charged particles are characterized by a well-defined **range.** This is the average penetration distance. It depends on the charge, the mass, and the velocity of the incident particle and on the material properties. Of these, the most important is the electron density in the traversed medium, which is related to the composition of the elements out of which the material is made.

The number of energy loss collisions suffered by heavy charged particles is very large, the statistical fluctuations will be relatively small, and all particles of a given kind, with the same initial energy, will stop very close to each other when all their energy is spent. Furthermore, while particles are still proceeding at high velocity, relatively little time is spent close to atoms, in which the attraction to atomic electrons is strongest; thus, energy losses are relatively small until the particle has slowed down considerably, near the end of its range. These facts are summarized in the plot of average relative ionization of a monoenergetic beam of particles, as a function of depth, as shown in Figure E.2. Such a plot is known as a "Bragg curve," after its discoverer. In Figure E.2, data are shown for two beams of iron particles incident on water, one incident at 600 MeV/nucleon and one incident at 1,000 MeV/nucleon. The data were obtained using the Brookhaven National Laboratory AGS accelerator. The range of the 600 MeV/nucleon iron beam is approximately 10 cm of water, whereas at 1,000 MeV/nucleon, the range is approximately 27 cm.

**Figure E.2. Bragg Curves for Monoenergetic Iron Beams**
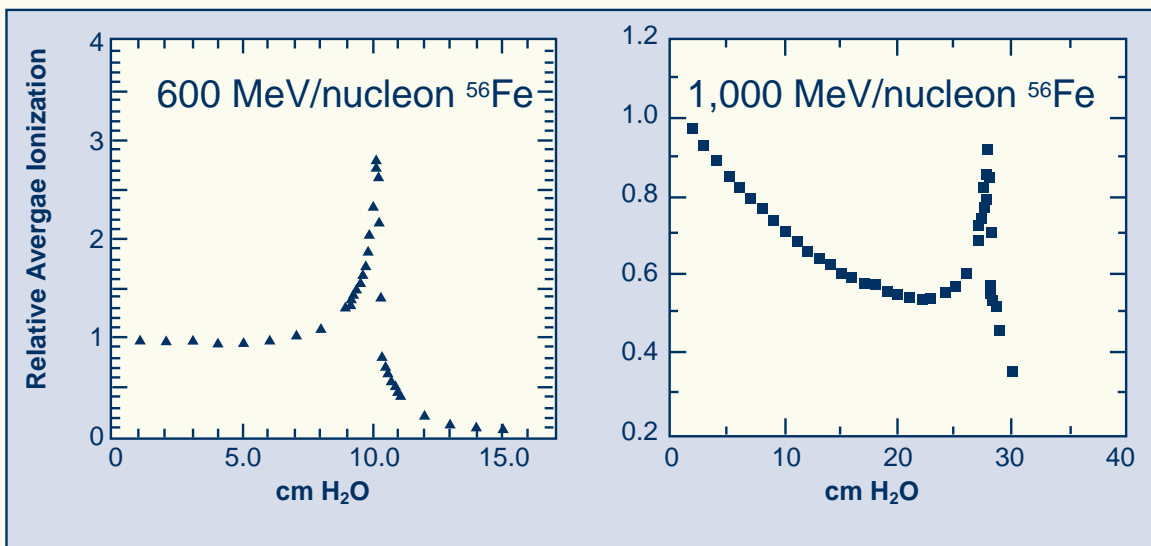
The theory of energy loss of charged particles in matter is well known. Given the charge and mass of a particle and the element composition of the target material, there is a relation among the energy loss per unit path length, the range, and the energy per nucleon (that is, the velocity) of the particle, such that, given any two, the third can be calculated. A sample of such calculations has been plotted in Figure E.3 for the nine most important components of space radiation in the energy region of interest.

Nuclear Interactions

The curves in Figure E.3 assume that the particles suffer no nuclear interactions. In the case of relatively low-energy beams, this assumption is a good approximation. However, in the case of high-energy beams, such as the 1,000 MeV/nucleon beam shown in the righthand Bragg curve of Figure E.2, this is no longer true. The range of such an energetic particle is large enough that loss of particles caused by nuclear interactions is significant. This accounts for the exponential decrease in the Bragg curve. However, even for the lower energy beam, there is a significant component of ionization from nuclear interaction products, and almost half the beam at the Bragg peak consists of secondary particles produced in nuclear interaction.

A significant fraction of the radiation flux traversing spacecraft components and in the bodies of personnel will undergo nuclear reactions. Nuclear interactions of charged particles are characterized by the probability of observing a given reaction outcome per incident particle fluence per reaction event. This is the cross section for the event, σ; it has the dimensions of an area presented to the incident particles. Commensurate with the size of the target nuclei, nuclear cross sections are usually given in units of barns (1 b = 10^{-24} cm^2). Typical nuclear reaction cross sections are given in millibarns (mb); by comparison, cross sections for atomic interactions are a million times larger. Cross sections can be a differential of energy, angle of the emerging products, multiplicity of observed particles, and other factors.

Figure E.3. LET Versus Range
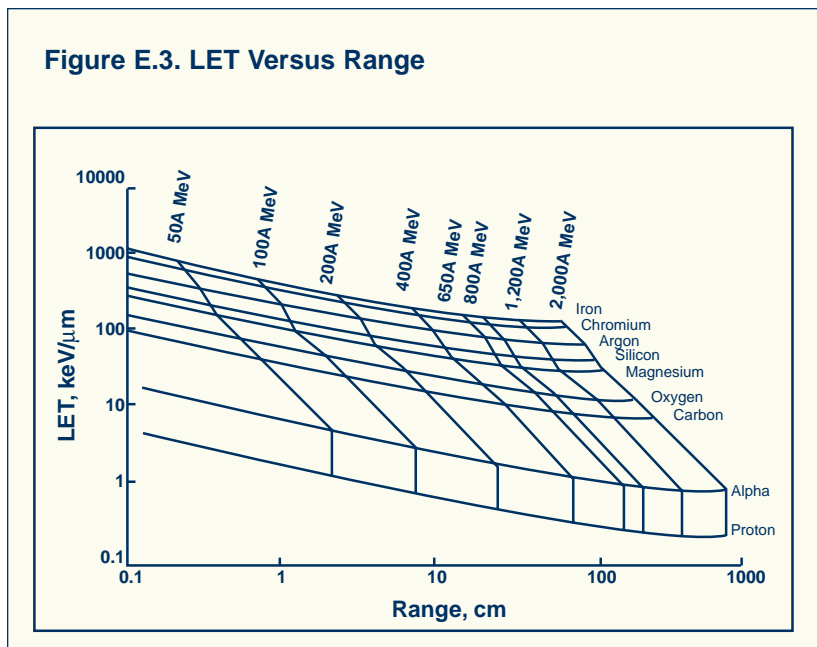
Nuclear interactions of the heavy component of GCR are usually classified into three categories: projectile fragmentation, target fragmentation, and central collisions. Seen from their respective rest frames, the products of projectile and target fragmentation are emitted with equal probability in all directions (that is, they are isotropic). However, in the (target) frame of reference of the shielded observer, the kinematics of relativistic particles are such that the projectile fragments will

APPENDIX E
INTERACTIONS OF PROTONS AND HZE

be sharply peaked forward in the direction of projectile incidence. Central collisions involve the overlapping region of the colliding nuclei, in which multiple collisions and regroupings of the participating nucleons lead to final products that can be emitted into much larger angles. A significant number of GCR interactions result in more than one high-energy particle emerging from the reaction. The multiplicity of GCR reaction products is related to the extent to which the collision is violent enough to break up the reacting nuclei or parts of them.

To characterize the radiation field to which personnel in space may be exposed, it is thus necessary to know the energy spectrum, the angular distribution, and the multiplicity of each type of secondary particle. In the cases of interest here, in which these reactions can take place anywhere in a thick absorber, it is necessary to know these quantities as a function of particle energy not only for all particles incident upon a thickness of material, but for all the particles produced inside the material as well.

The theory of nuclear reactions of HZE particles is much less developed than other parts of high-energy nuclear physics. In part, this is because high-energy heavy particle beams have only become available relatively recently; in part, it is because the number of possible outcomes in any given nuclear reaction is enormously larger than is usual for lower energies or simpler protons and neutrons. To some extent, the nuclear reactions between HZE particles, at very high energies, are also a field in which new ideas of physics are being developed, such as the search for a quark-gluon plasma, for which the new Relativistic Heavy Ion Collider at Brookhaven is intended.

Appendix F
Elementary Concepts of Radiobiology

Dosimetry

As noted in Appendix E, biological effects are caused by the disruption of chemical bonds when radiation is incident on tissue. To a first approximation, this is proportional to the energy absorbed per unit volume. The **absorbed dose,** usually referred to simply (but inappropriately) as **dose,** is the average energy deposited per unit mass inside a small volume. The volume must be small enough for the average energy to be constant. It must also be large enough to contain many molecules or cells so that statistical fluctuations in energy deposition are not significant. The **dose rate** is the rate at which this energy is being deposited, or dose per unit time. For charged particles, it is equal to the dose per particle times the number of particles traversing the target volume per unit time.

In most situations of interest, the deposited energy is closely related to the energy lost by the incident particles. However, this may not always be the case. For example, high-energy electrons are produced by charged particles traversing a cell. These high-energy electrons may escape, depositing their energy in other locations, outside the cell. At low dose rates, only one or a few particles are likely to traverse a cell, and the energy deposited in the cell is less than the energy lost by the particles. However, when a large number of particles is present, then electrons generated outside the cell may compensate for those that are lost. Thus, the concept of absorbed dose incorporates many assumptions and approximations that disciplines such as *microdosimetry* attempt to address. Nevertheless, the approximations are good enough that dose is used as the basis for estimating risk for x-rays and gamma rays. For historical reasons, x-rays have been used as the standard reference radiation with which all other types of radiation have been compared. The unit of absorbed dose is the Gray (Gy); it is equal to an average energy deposition of 1 Joule per kilogram (J/kg). An older unit, the rad, enjoys fairly frequent unofficial usage (one Gy is equal to 100 rad).

As was seen in Appendix E, heavy charged particles deposit energy at a very high density—high LET—which can be thousands of times higher than that deposited by x-rays and gamma rays (often referred to as low-LET radiation). The electrons released in tissue by x-rays have mean LET values of 2 to 3 keV/μm, while the gamma ray sources have mean LET values in the range of 0.2 to 0.5 keV/μm. While low-LET secondary electrons can pass through the spacing (approximately 3 nm) between DNA strands without interacting, some high-LET ions can produce an ionization trail so large that it inactivates nearly every cell it traverses.

For heavy charged particles, however, different types of radiation do not produce the same observed effect at the same observed dose. This is to be expected because the microscopic distribution of deposited energy and, hence, the chemical processes deriving from it, are not the same even though the average energy deposition (the absorbed dose) may be the same. The differences in biological action for different types of radiation at the same absorbed dose are known as the "quality" of the radiation.

In the field of radiation protection, the *dose equivalent,* H, has been used to normalize biological damage to that of x-rays, by means of the relationship H = QD, where Q is the quality factor defined as a function of LET. The unit of dose equivalent is the Sievert (Sv), where 1 Sv is presumed, for the purposed of radiation protection, to have the same biological consequences as 1 Gy of x-rays.

Cells and Tissues

The basic unit of the living organism is the cell. The interior of cells is highly organized. Mammalian cells, as opposed to bacterial cells, have a central core, the nucleus, separated from the rest of the cell by a semipermeable membrane. The cell itself is contained in a similar membrane, which is usually negatively charged on the outside and positively charged on the inside. Surface charges are sustained by layers of lipid molecules (soluble fats) in the membrane. Charged and neutral atoms and molecules can be transferred by passive transport through pores or active transport through the folds of proteins embedded in the membrane.

Within the cell, the deoxyribonucleic acid (DNA) molecules contain the information required for the synthesis of intracellular proteins, for cell reproduction and for organization of the tissues and organs. Other cellular structures participate in cellular function, but DNA is by far the component most sensitive to radiation, and, hence, the action of radiation on living cells is most often considered on the basis of the interaction of radiation with DNA.

Cells divide under the control of chemical signals provided by their environment, including molecules generated by other cells. During development of an organism, the dividing cells differentiate into tissues and organs. Some adult tissues maintain "pluripotent stem cells," which, when stimulated to divide, can replenish depleted tissues, such as blood or the intestinal lining. Cell division takes place in a well-defined **cell cycle,** consisting of a resting stage, a stage in which DNA is synthesized to provide double the original amount, a further resting stage, and a stage in which actual division of the cell into two daughter cells takes place. In the adult organism, most cells are shunted aside into a longer resting stage that does not involve continued proliferation.

Cell death in biological systems can be separated into two distinct forms: necrotic death and programmed death or apoptosis. Cell death is defined generally as loss of reproductive ability, because seriously damaged cells are often able to continue to function, as long as the chemical sites involved in this function are not themselves damaged by the radiation. Cell survival is an endpoint best measured in the laboratory as the ability of cells to divide into colonies; in living organisms, cell death only becomes manifest when the function of an organ or tissue is impaired.

The cell cycle is monitored by a multitude of chemical control systems. A major component of cellular defense against DNA damage consists of cell cycle checkpoints—that is, monitoring systems for DNA damage that temporarily halt transcription (the synthesis of RNA leading to protein synthesis) and/or repli-

cation (the synthesis of DNA) until the damage (referred to in general terms as "lesions") is repaired. When defects in DNA cannot be repaired, or are too extensive, the cell cycle control system can induce apoptosis in the cell and eliminate it.

The expression of damage in tissue is complicated by the presence of up to 50 cell types per tissue, and by the interactions among them. Homeostasis (the requirement to keep the properties of the internal environment of the organism within operating limits) is maintained through a web of soluble growth factors and hormones, insoluble extracellular matrix components, and cell surface receptors that communicate these signals to individual cells as well as between cells. Research questions need to be addressed, wherever possible, at the tissue level rather than in cell culture, so that the influence of the microenvironment can be assessed.

Radiation Effects

The diameter of a mammalian cell is typically of the order of 0.001 inch. The nucleus can take up anywhere between 10 and 90 percent of the cell's volume. Inside the nucleus, the DNA is tightly wound into a tiny double helix, 100 times smaller than the cell. Thus, the passage of sparsely ionizing radiation, such as x-rays, is not likely to result in frequent, direct ionization of even one bond on a DNA molecule. Radiation effects on the DNA are more likely to occur because molecules in the surrounding material, principally the surrounding water, have become ionized and, hence, chemically very reactive. When such molecules diffuse close enough to the DNA, they may undergo chemical reactions that can significantly alter the information stored in the DNA or its function. However, the densely ionizing central region of a charged particle traversing the cell has dimensions comparable to that of the DNA molecule. The passage of such a particle can cause one or more ionizations in every single DNA molecule it traverses. When the incident radiation deposits energy directly in the target DNA molecules, the process is referred to as a "direct" effect.

Of all the mechanisms resulting in initial damage to DNA, strand breaks are the most important. Breaks in a single strand are repaired efficiently by intracellular repair mechanisms. Double-strand breaks can occur as two neighboring single-strand breaks caused by direct action or as the result of the interaction of two independent single-strand breaks, separated by less than a critical distance. The magnitude of that distance is not known at present. Double-strand breaks are repaired much less efficiently than single-strand breaks and are much more likely to lead to cell death.

The modification of cell function can result from nonlethal changes in DNA leading to either benign or malignant cell proliferation ("neoplastic transformation"). This is an initial event in a sequence leading to cancer. A schematic depiction of the possible pathways leading from this event to uncontrolled proliferation and, possibly, cancer is shown in Figure F.1. Further events, resulting from subsequent radiation or stimulation by so-called promoting substances, need to take place before the cell can be considered "precancerous." Precancerous cells may not always lead to cancer; further changes in the cell and surrounding tissues are required for this so-called "progression" stage. Even in the absence of cancer initiation, permanent changes

APPENDIX F
CONCEPTS OF RADIOBIOLOGY

in cellular DNA may occur as mutations. Such mutations, when they occur in reproductive cells, may become inheritable and manifest in the progeny of the irradiated organism. These changes, in a cell that has maintained reproductive integrity, are known as "genetic effects."

The effects of radiation action are measured, according to the different endpoints, in terms of number of colonies formed by surviving cells, number of cells manifesting a measured change, probability of tumor formation, and so forth. The effects are also time dependent, as shown in Figure F.2. Proliferative tissues, in which cells divide relatively rapidly (for example, the intestinal lining and blood cells), will show a fairly large initial damage from cell killing but will also recover rapidly if cells are available to replenish the tissue loss. Nonproliferating or slowly proliferating tissues will show damage slowly, as cells die off, but will not show recovery because there are no dividing cells to replenish the tissue. Late effects, caused by accumulated genetic damage in surviving cells, can occur in both cases.

From the point of view of radiation protection, effects fall into two categories. When the effects are certain to be seen in the irradiated individual, they are called "deterministic." Relatively large doses of radiation are required to cause such effects, because the organism has the means to compensate for tissue damage. However, once an individual threshold is exceeded, the severity of the effect increases with increasing radiation dose. Examples of **acute** or early deterministic effects are skin reddening or radiation burns, as well as nausea or vomiting caused by the destruction of cells in the intestinal lining. Examples of **chronic** or late deterministic effects are lens opacification (cataracts), organ atrophy, and a decrease in germ cells leading to sterility. The threshold in which the destruction of nonproliferating brain cells leads to measurable changes in behavior is not known.

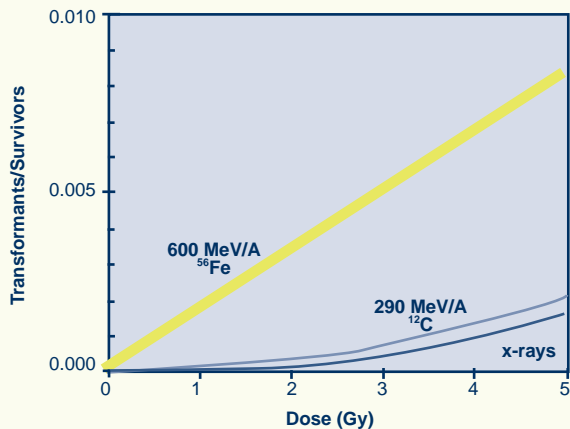**Figure F.1. Pathways for Radiation Effects on Single Cells**
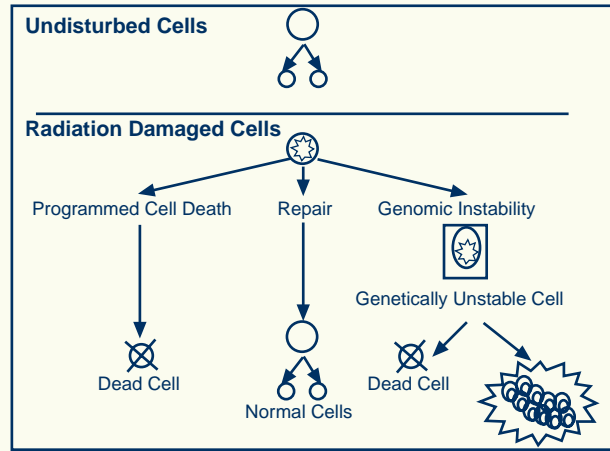
Figure F.2. Time Course of Radiation Response for Proliferative (a) and Nonproliferative (b) Tissues
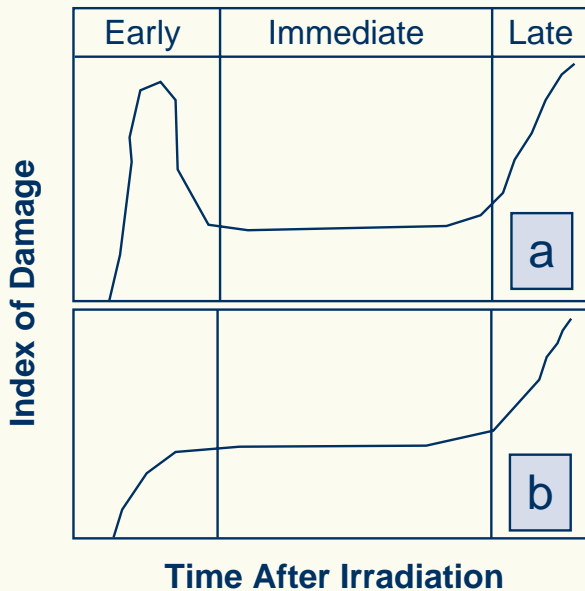
Figure F.3. Survival of 10T1/2 Cells
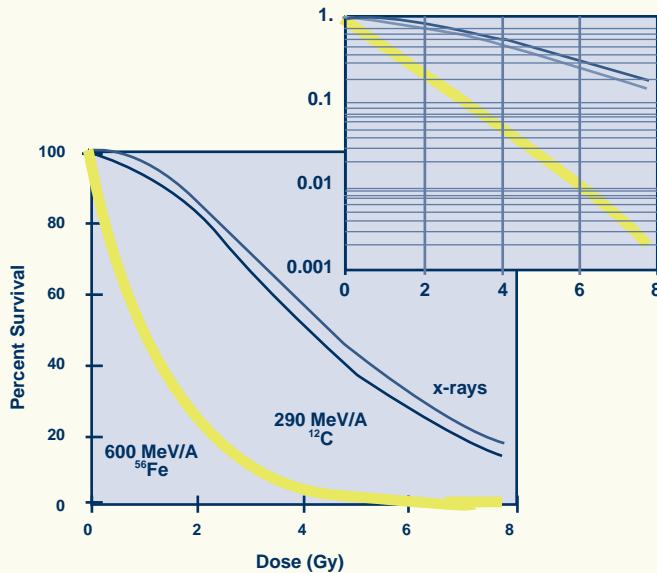
Note: The scale in this figure is linear, to make it more accessible for nonspecialists. The data are usually presented to specialists as semi-logarithmic plots, shown in the inset.

Figure F.4. Transformation of 10T1/2 Cells

When the effects of radiation exposure on the exposed individual cannot be predicted, so that there is a probability but no certainty of a given effect, the effect is called "stochastic." Stochastic effects arise at the cellular or subcellular level and lead to an all or none response, such as the induction of cancer or of mutations leading to genetic effects. The probability of the effect increases with absorbed dose, but the severity of the effect (such as death) is not related to dose. The induction of stochastic effects is considered to be the principal consequence of low doses of ionizing radiation and, in general, is delayed relative to the time of exposure. These distinctions reflect differences between cellular effects and tissue effects, as illustrated in Figures F.3 and F.4.

Figure F.3 is a model calculation of cell survival. The model is based on experimental measurements of survival of cells in culture. Figure F.4 is a similar calculation for "transformation"—that is, the loss of some characteristic, such as contact inhibition, thought to be indicative of an initial, possibly precancerous state. The survival of cells irradiated by x-rays has a broad shoulder, which is generally attributed to the capacity of cells to repair radiation damage. In this case, the cells whose response is modeled were allowed to grow in culture before being fixed for study. Densely ionizing particles, such as iron nuclei, cause so many lesions in the DNA of a cell that no repair can be seen to occur. Intermediate ionization, such as that caused by carbon ions, does not result in significant repair, but is also less efficient at killing cells.

Surprisingly, not all cells traversed by charged particles, even ones as heavy as iron nuclei, are killed. Some of the cells are transformed. In culture, precancerous transformation increases in direct proportion to dose. As would be expected, high-LET iron is much more effective than high-LET C nuclei or low-LET x-rays. There is only one set of heavy-ion data available for actual tumor induction in tissue. These data
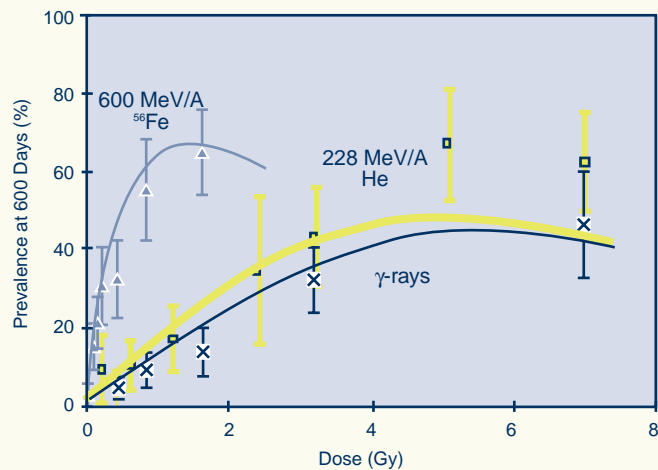
were obtained for tumor prevalence (the probability of observing a tumor at a given time after irradiation) in the Harderian gland of mice and are plotted in Figure F.5. A high tumor prevalence can be seen at relatively low doses of iron. Furthermore, the response is not proportional to the dose but increases in a nonlinear way. The decrease in tumor prevalence beyond the maximum is probably because too many cells are damaged, or they are damaged beyond the capabilities of the organism repair system, and simply do not survive.

From considerations such as the above, it is clear that different types of radiation do not result in the same type of effect. In Figure F.4, inducing a level of 0.001 transformed cells per surviving cell requires 4 Gy of x-rays, but only 1 Gy of iron; the iron is four times as effective as x-rays. In Figure F.5, a 30-percent prevalence of Harderian tumors is the result of approximately 3 Gy of gamma rays, but of only 1 Gy of iron; in this case, the iron is approximately three times as effective as gamma rays. This ratio of doses to produce the same effect describes the **relative biological effectiveness,** or **RBE,** of different types of radiation; to a first approximation, it is a function of LET. It is used to describe the "quality" of the radiation.

Figure F.5. Prevalence of Harderian Gland

Figure F.6. Relative Biological Effectiveness for 10T1/2 Cell Transformation
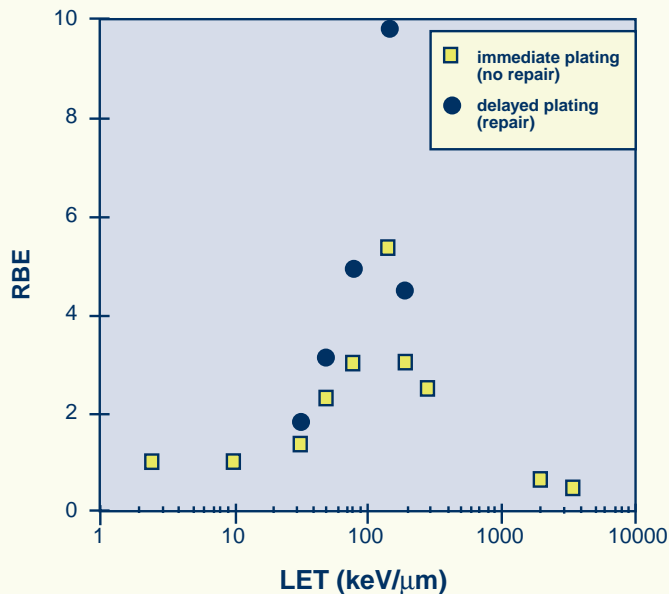

Figure F.6 illustrates the dependence of RBE on LET for the transformation of a mouse cell; for other cell systems in culture, the RBE has a similar shape. It increases with LET up to a peak around 100 keV/μm and then decreases rapidly. This behavior has also been found for tissues in culture. For Harderian gland tumor prevalence, however, the RBE has been found to remain at a value of approximately 30 for particles between iron and niobium.

This behavior, in the case of cells in culture, is attributed to the fact that the probability of inducing the observed effects increases with LET, for high-LET particles, but that the efficiency of x-rays to produce sim-

Table IV. Relative Contribution of Individual Tissues and Organs to the Probability of Fatal Cancer

(in units of percent probability per Sv)

Tissue	Males	Females
Breast	—	0.70
Respiratory System	1.90	1.50
Digestive System	1.70	2.90
Other Solid Tumors	3.00	2.20
Leukemia	1.10	0.80
Total	7.70	8.10

Note: BEIR V data summarized in Hall, Eric J. *Radiology for the Radiologist*, 4th ed. (Philadelphia, PA: J.B. Lippincott Co., 1994).

ilar effects, especially at low doses, is considerably diminished. Thus, the ratio of x-ray dose to particle dose that defines LET decreases, reflecting the x-ray inefficiency. From a different perspective, the high ionization density at the core of a particle path means that, at a microscopic level, HZE particles do not deposit energy at a low dose; they only deposit very high doses in very small volumes, so that the average seems to be lower than the biological effectiveness would warrant.

A further indication of the dependence of radiation effect on tissue is shown in Table IV, in which the relative contribution of individual tissues to the probability of fatal cancer has been listed. It is clear that some tissues are more sensitive than others to initial damage, have different mechanisms for the repair, repopulation, and replacement of damaged cells, and offer different access for treatment.

The above considerations underlie the set of critical questions that are listed in Appendix H. They address the knowledge required for accurate predictions of radiation effect and, accordingly, for devising accurate radiation limits.

Radiation Transport

Shielding is the use of materials to mitigate the effects of incident radiation, by reducing the intensity of the radiation inside the shielded volume, by changing the deleterious properties ("quality") of the radiation, or both. Examples of reducing the intensity of radiation are: attenuation of x-rays by absorption of photons in a lead curtain; attenuation of neutrons by nuclear interactions in hydrogenous materials; and stopping of high-energy heavy ions in lunar regolith. Examples of changing radiation quality are: moderation of neutrons in hydrogenous materials, which changes their energy but not their number, and projectile fragmentation in spacecraft shielding, which results in lighter pieces of the incident projectile with less ionization density (LET).

Most shielding materials will change the energy, direction, and kind of particles comprising the radiation field. The iron Bragg curves of Figure E.2 show how the relative dose decreases in a water absorber. This decrease is caused by a combination of effects. On the one hand, incident iron nuclei suffer nuclear interactions. In some of these nuclear interactions, parts of the iron nuclei are emitted approximately in the same direction and with the same velocity as the incident nucleus. These parts are lighter nuclei with lower charge Z (fewer protons), and they ionize less, proportional to Z^2. In other reactions, the nuclei of iron may fragment entirely and be removed from the stream of particles. On the other hand, the iron nuclei and the nuclear interaction products that do not interact continue losing energy. The slower particles have greater LET, resulting in higher relative doses. Finally, near the end of their range, the particles stop and are removed from the radiation field; the heaviest particles with the highest charge lose most energy and are stopped first.

Shielding materials are generally "thick" materials, in the sense that they present enough matter to the incident material so that the energy losses of incident charged particles can be large (to the point of stopping in the material) or multiple nuclear interactions can occur to successive generations of secondary particles. The calculation of the number of particles and of their kinds, energies, and directions inside or behind any material is known as a "radiation transport" calculation. It is the means to predict how the radiation environment external to any human habitat is transformed by the presence of the materials of which the habitat is constructed.

Radiation transport calculations require accurate accounting, at each generation of interactions, of each particle's change of identity, energy, and direction. In the case of neutrons, in which the number of particles is small and the different kinds of particles are limited, Monte Carlo methods have been used to make such calculations. In a Monte Carlo calculation, random numbers are generated for the particle position, energy, and direction, and the probability of a nuclear interaction is computed, yielding a set of numbers describing the particle's new energy, position, and direction. This particle is followed until it is removed

from the radiation field, and a similar computation is started for the next particle. If very large numbers of particles need to be simulated, Monte Carlo calculations can take a very long time and be very costly.

For modeling the transport of nucleons (neutrons and protons) through arbitrary target materials, a deterministic nucleon (BaRYoN) TRaNsport code, named BRYNTRN, has been developed by NASA at the Langley Research Center. The current version of the code accepts continuous spectral distributions from SPE/GCR protons as input. For modeling the transport of GCR (nucleons and HZE particles) and their reaction products through arbitrary target materials, NASA uses a deterministic HZE TRaNsport code, named HZETRN. Computer codes for the propagation of GCR also exist in Russia and Europe.

Shield Material Characteristics

Desirable shielding materials will result in high energy loss (stopping power) by the incident particle, while at the same time resulting in a low probability of nuclear interactions that might lead to projectile fragments. Because energy loss depends on the number of electrons while nuclear interactions depend on the number of nucleons, the best shielding materials are likely to be those that have the highest ratio of electrons to protons. Hydrogen, with exactly one electron and a one-proton nucleus, has an electron/proton ratio of

Figure G.1. Primaries and Secondaries Inside 5 g/cm² of Aluminum

Dose Equivalent (skin)

Harderian Gland

C3H10T1/2 Cell Death

C3H10T1/2 Cell Transformation
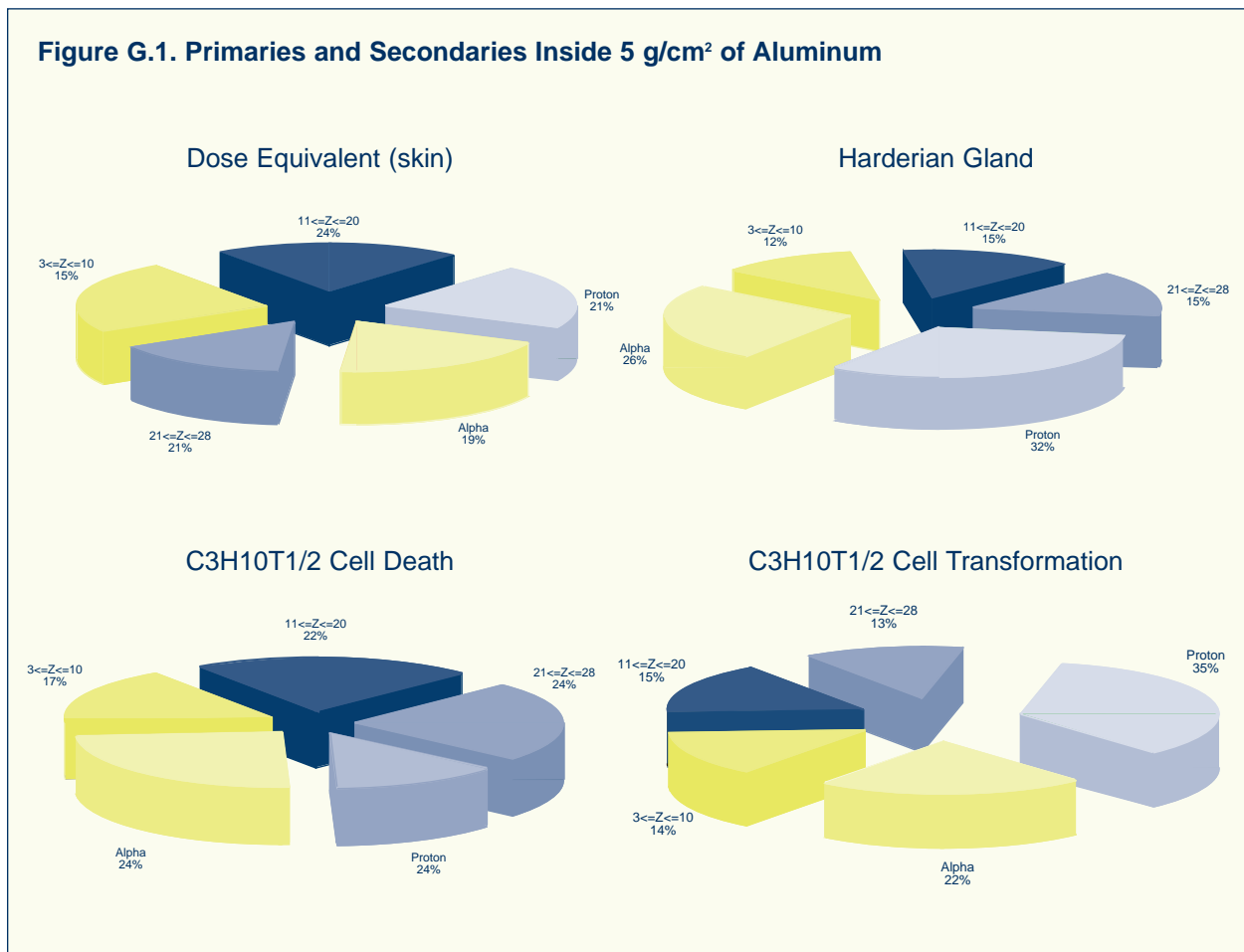
1, higher than that for any other element, and it is thus the most desirable component to use in shielding materials. Wilson and his colleagues at Langley Research Center have done extensive analyses of hydrogen-containing materials. A discussion of their structural and other properties and of the issues involved in shielding optimization can be found in the workshop report "Shielding Strategies for Human Space Exploration."

The results of a conventional radiation transport calculation specify the physical characteristics of the radiation field inside or behind shielding. However, to estimate risk, it is necessary to calculate the dose, dose equivalent, or other properties of the radiation field. As illustrated in Figure G.1, the contribution of the various particle species inside 5 g/cm^2 of aluminum shielding is different for different biological endpoints, illustrating the requirement to characterize shielding efficacy in biological terms. As shown by Wilson and his colleagues, the biological characterization of shielding accentuates features not clearly distinguishable by the use of conventional dose equivalent. Biological figures of merit are required for shielding optimization.

Appendix H
Critical Questions

Space Radiation Environment

- For a given mission, what are the fluxes of galactic cosmic rays (GCR) in interplanetary space as a function of particle energy, LET, and solar cycle?

- What is the solar cycle dependence of space radiation?

- What is the trapped radiation flux as a function of time, magnetic field coordinates, and geographical coordinates?

- What are the maximum flux, the integrated fluence, and the probability of large solar particle events (SPE) during any mission?

- What are the doses related to heavy ions in deep space?

- What are the factors that determine the radiation flux of SPE?

Nuclear Interactions

- What are the cross sections and yields for nuclear interactions of HZE particles in tissue and shielding materials?

- What are the angular distributions of nuclear interaction products?

- What are the particle multiplicities of nuclear interaction products?

- How is a radiation field transformed as a function of depth in different materials?

- What are the optimal ways of calculating the transport of radiation through materials?

Atomic Interactions

- What is the precise energy deposition of heavy ions?

- What are the yields and energy spectra of electrons?

- How can the wealth of knowledge existing for energy deposition in gaseous media be extended to the liquid phase applicable to most living cells?

- How do diffusion, recombination, and other interactions of chemical intermediaries alter the chemical events at the DNA level?

- How is physical energy deposition related to biological effect?

Molecular Biology

- What are the probabilities of GCR to produce radiation damage at specific sites on DNA?

- How are processes such as oncogene activation and oncogene suppressor inactivation involved in the carcinogenic effects of GCR radiation?

- What mechanisms are involved in modulating radiation damage at the molecular level (repair, errors in repair, gene amplification, and so on)?

- How can molecular mechanisms of radiation damage be used to understand effects in whole cells?

- What are the sizes of molecular lesions relative to functional units on DNA, as a function of ionization density?*

- Can early molecular changes be used to predict the probability of subsequent carcinogenic effects?*

Cellular Biology

- What is the probability of initiating neoplastic cell transformation or other steps leading to a cancerous cell?

- How do cellular repair mechanisms modulate damage produced by energetic charged particles?

- How can the radiation effects on cells in culture be related to radiation effects in "normal" cells and tissues?

- How can cellular mechanisms of radiation damage be used to understand effects in whole organisms?

- What is the nature of genomic instability caused by heavy charged particle radiation?*

- Could a single particle take out a multiple stem cell?

- Can unique effects (such as totally exploded chromosomes) be produced with low probability by some HZE particles?*

Animal Models

- How can animal models be used to extrapolate probabilities of radiation risk to humans in space?

- What is the relative biological effectiveness of different types of radiation for the relevant endpoints such as cancer and cataracts?

- How can protection against the effects of GCR and the proton radiation of solar events be improved?

- What is the age dependence of relevant radiation effects in animals (cancer, cataractogenesis, life shortening, and so on)?

- Are there qualitative differences between lesions and tumor characteristics induced by HZE particles and those induced by x-rays?*

Humans

- What should be the radiation dose limits for manned deep space missions?

- What is the probability of cancer as a function of dose, dose rate, radiation quality, gender, age at exposure, and time after exposure?

- What is the effect of GCR at different stages of the carcinogenesis process?

- What is the probability of cataract formation as a function of the same quantities?

- What is the probability for genetic and developmental detriment incurred as a consequence of radiation exposure in space?

- How are risks associated with acute exposure to space radiation to be managed medically?

- What pharmacological agents should be developed and tested as prophylactic agents for low LET?

- What will the radiation environment be within the space vehicle, and what factors influence the flux, energy, and linear energy transfer spectra of the radiation?*

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* Added subsequently

APPENDIX H
CRITICAL QUESTIONS

Appendix I
## Ground-Based Particle Accelerator Facilities

Ground-based accelerator exposure facilities provide beams of protons and HZE particles at energies within the range of space radiation. The main purpose of simulating space radiation at these facilities is to determine the biological factors of risk. However, they can also be used to obtain required data on the physical interactions of these beams with materials and space instruments. Data about the interaction of HZE particles with materials is required especially for the design of lightweight optimized shielding config-urations. The calibration and design of instruments is required to interpret reliably the data about the space radiation environment collected on the Space Shuttle, *Mir,* and the ISS, in robotic precursor missions, and through other assets.

The facilities available for simulation of space radiation are severely limited. While proton beams can be produced at many facilities, currently only the Loma Linda University Therapy Proton Synchrotron facility is equipped to handle the sophisticated biological research required for radiobiological studies simulating protons in space.

The situation for HZE simulation is even more constrained (Figure I.1). There are only four facilities con-sidered practical for use by this program. One of these, the heavy ion accelerator SIS at the GSI research

Figure I.1. Cumulative Yearly Dose Equivalent From HZE Particles
(In three charge groups, up to energy per nucleon E, for blood-forming organs behind 5 g/cm^2 of aluminum - bands - compared with capabilities of three accelerator facilities)
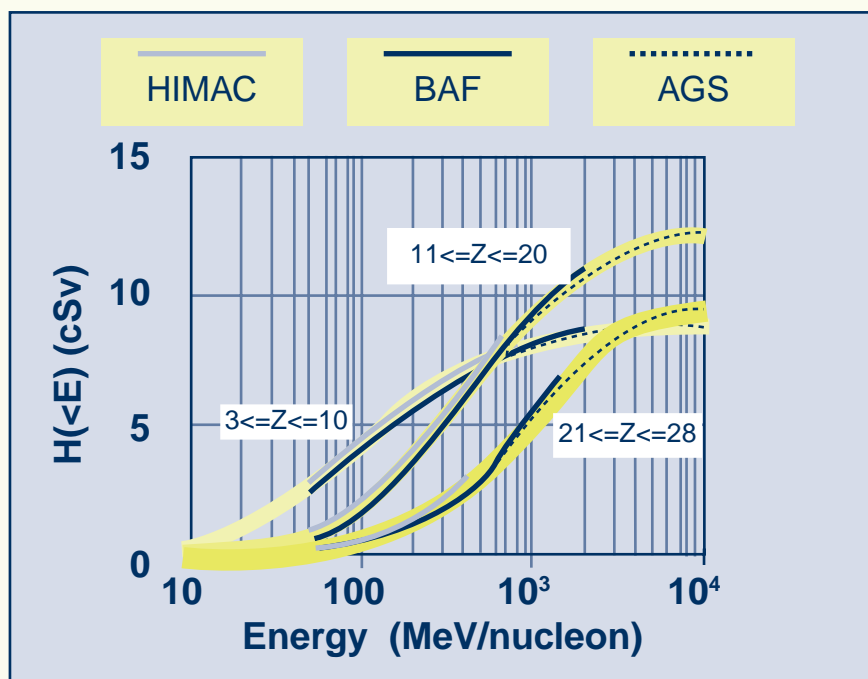
institute in Darmstadt, Germany, is in high demand by the German nuclear physics community. In addition, the use of the facility for cancer therapy started in December 1997, and the facility can be considered unavailable for all intents and purposes. The HIMAC facility at the National Institute of Radiological Sciences in Chiba, Japan, has a moderate amount of beam time available, and an active collaboration between the NASA Space Radiation Health Program and this laboratory has been under way since 1995.

Figure I.2. Accelerator Facilities at Brookhaven National Laboratory
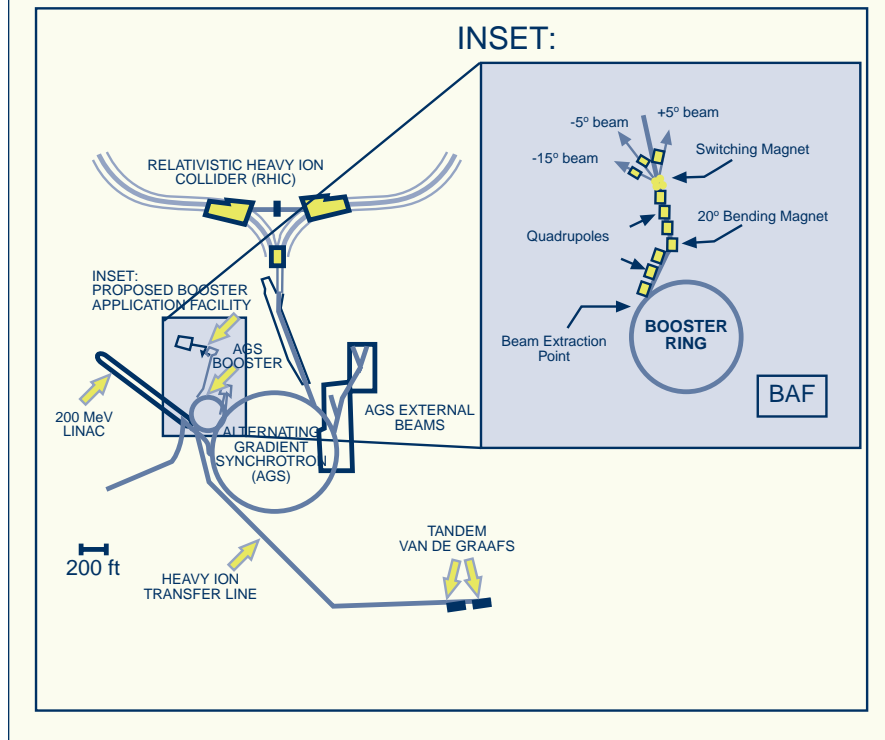
The other two facilities for HZE delivery are the Alternating Gradient Synchrotron (AGS) at Brookhaven National Laboratory (BNL) in Long Island, New York, and the Booster Synchrotron, used as an injector in the accelerator chain leading to the AGS (Figure I.2). These accelerators are currently operated by the high-energy and nuclear physics programs of the Department of Energy, and NASA purchases beam time for several experimental campaigns per year. As of the writing of this Plan, four campaigns of 150 hours each, denoted by BNL-1 through BNL-4, have been successfully accomplished.

Protons originate with the LINAC injector, and HZE particles originate in one of the two Tandem Van de Graaffs. The Booster Synchrotron then accelerates particles for injection into the AGS, in which they are accelerated further for injection into the Relativistic Heavy Ion Collider (RHIC).

Currently, experimenter access to the Booster Synchrotron is not available. A suitable irradiation facility, the Booster Applications Facility (BAF), has been designed and reviewed. Its construction is an integral part of the Space Radiation Health Program. A proposal to build and operate the BAF was prepared by BNL and has been reviewed by a NASA Facilities Panel, a NASA/Department of Energy Interagency Panel, and a Department of Energy Technical Review Panel. The reviews agreed that the proposal was appropriate and technically sound and that the budget was reasonable.

Construction of the BAF is constrained by RHIC operation. For this reason, the BAF proposal contemplates commissioning the second Van de Graaff (to provide a source of particles independent of the ones used for the RHIC) and constructing early tunnel penetration into the Booster shielding vault. *The above considerations make access to the Loma Linda and Brookhaven facilities, as well as the construction of the BAF's essential elements, without which the Space Radiation Health Program cannot proceed.*