

POTENTIAL IMPACT OF INDIVIDUAL GENETIC SUSCEPTIBILITY AND PREVIOUS RADIATION EXPOSURE ON RADIATION RISK FOR ASTRONAUTS



Potential Impact of Individual Genetic Susceptibility and Previous Radiation Exposure on Radiation Risk for Astronauts

**Recommendations of the
NATIONAL COUNCIL ON RADIATION
PROTECTION AND MEASUREMENTS**

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**National Council on Radiation Protection and Measurements
7910 Woodmont Avenue, Suite 400 / Bethesda, MD 20814-3095**

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Preface

The National Council on Radiation Protection and Measurements (NCRP) has provided guidance to the National Aeronautics and Space Administration (NASA) in several reports related to astronaut radiation protection and operational radiation safety during missions in low-Earth orbit (LEO). These reports include NCRP Report No. 98, *Guidance on Radiation Received in Space Activities* (1989); NCRP Report No. 132, *Radiation Protection Guidance for Activities in Low-Earth Orbit* (2000); and NCRP Report No. 142, *Operational Radiation Safety Program for Astronauts in Low-Earth Orbit: A Basic Framework* (2002). Further, NCRP has held conferences and prepared several publications on specialized topics related to NASA space activities. These include Symposium Proceedings No. 3, *Acceptability of Risk from Radiation – Application to Human Space Flight* (1997) and Annual Meeting Proceedings No. 20, *Cosmic Radiation Exposure of Airline Crews, Passengers and Astronauts* (2000). In addition, other publications of relevance to the NASA space program are NCRP Commentary No. 12, *Radiation Exposure and High-Altitude Flight* (1995); NCRP Report No. 131, *Scientific Basis for Evaluating the Risks to Populations from Space Applications of Plutonium* (2001); NCRP Report No. 137, *Fluence-Based and Microdosimetric Event-Based Methods for Radiation Protection in Space* (2001); and NCRP Report No. 153, *Information Needed to Make Radiation Protection Recommendations for Space Missions Beyond Low-Earth Orbit* (2006). NASA also contributed to NCRP Report No. 151 on *Structural Shielding Design and Evaluation for Megavoltage X- and Gamma-Ray Radiotherapy Facilities* (2005).

This Report addresses additional questions related to the radiation protection of NASA astronauts in LEO, lunar and interplanetary missions. The Report discusses whether genetic susceptibility factors or prior radiation exposures can influence the radiation health risks for astronauts resulting from radiation exposures that occur during space missions over the course of their lifetimes. With current technology, it is generally not possible to predict an individual's inherent genetic susceptibility to the long-term risk of cancer or other diseases associated with radiation exposure. However, it is anticipated that the results of ongoing and future medical research will lead to an ability to predict the effects of genetic susceptibility

on lifetime risk of stochastic diseases. Similarly, it is expected that the influence of prior radiation exposures (*e.g.*, from medical procedures) may be better understood as a result of current and future research on exposed populations. This Report addresses the scientific basis for projecting the impact of these important factors in establishing radiation health protection guidance to reduce the risks associated with future space missions of NASA astronauts. The Report also discusses the legal, ethical and regulatory issues associated with using information on genetic susceptibility and prior radiation exposures to predict an astronaut's lifetime radiation-related health risks.

This Report was prepared by Scientific Committee 1-13 on the Potential Impact of Individual Susceptibility and Previous Radiation Exposure on Radiation Risk for Astronauts. Serving on Scientific Committee 1-13 were:

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Antone L. Brooks

Washington State University
at Tri-Cities
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Thomas S. Tenforde
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Executive Summary

This Report was prepared to evaluate the potential impact of individual genetic susceptibility and previous radiation exposures on radiation associated health risks for astronauts during their lifetimes following space missions.¹ The Report also evaluates whether either of these factors needs to be included in the radiation protection program for astronauts.

With the development of techniques to sequence the human genome, the science of genetics has advanced rapidly over the past few years. Using these sequencing techniques, it may become possible in the future to determine the genetic background of individuals and thus to better understand individual risk and the mechanisms involved in radiation-related cancer. With current genetic techniques, it is possible to define many different mutations involving numerous known genes that may alter an individual's lifetime risk for radiation-induced cancer. Linking research on genetic background to radiation sensitivity may pave the way to predicting an individual's radiation-related risks and thus improve radiation protection guidance. Currently, this is not possible as all risk estimates are derived from large populations. The information available on the impact of genetic background on risk and its future potential is one of the major subjects addressed in this Report.

Another major purpose of this Report is to determine whether the risk associated with past radiation exposures from medical therapy or diagnostic procedures is altered by radiation exposure during space exploration. Whether to include nonoccupational exposure in evaluating total lifetime risk limits set by the National Aeronautics and Space Administration (NASA) is discussed. It was determined that such exposures should not be added to occupational exposures. It should be recognized that in population studies, risk estimates incorporate all sources of radiation that the population receives, whether natural background or medical, as part of the background exposure, albeit the magnitude is not known. Thus, the risk estimates that are derived are those that are above the normal population exposures to these other sources. This

¹In the context of this Report the term "space missions" includes low-Earth orbit, lunar and interplanetary missions.

Report includes an evaluation of the regulatory, legal and ethical issues associated with using information on radiation-related genetic background and previous radiation exposures to predict an individual's lifetime radiation risk.

The following is a summary of the primary conclusions reached in this Report:

- Evaluation of genetic susceptibility to radiation-induced cancer and the influence of prior radiation exposure (*e.g.*, from medical therapy) should be given consideration as factors that could influence the long-term risk of cancer and other health effects in astronauts resulting from exposure to radiation received during space missions. However, at this time it is not possible to make accurate predictions of future risks associated with genetic susceptibility.
- NASA focus on health risk-based criteria for evaluating the safety of astronauts is consistent with the need to better understand the role of other factors such as genetic susceptibility and prior radiation exposures in evaluating the health risk to astronauts from estimated radiation exposures that may occur during planned space missions. The radiation risk level should not exceed a 3 % increase in lifetime risk of fatal cancer.
- There have been extensive laboratory studies on the role of genetic susceptibility in radiation sensitivity of cellular and tissue model systems. However, with the exception of a relatively small fraction of the human population that is known to have innate genetic susceptibility to cancer from radiation exposure, it is difficult if not impossible at this time to use the available information to make predictions on the role of genetic factors for the small corps of astronauts participating in space exploration.
- In addition to an increasing amount of laboratory data that are being obtained on carcinogenic effects from acute and chronic exposure to both low and high linear-energy transfer (LET) radiations, extensive data also are available from atomic-bomb survivors, medical patients and workers exposed primarily to low-LET radiation. However, because of the unique space radiation environment that involves low- and high-LET radiations, there is nonetheless a limited body of information on which to make precise predictions of astronauts' long-term risks of cancer and noncancer diseases resulting from radiation exposures in space missions.
- Important factors in analyzing the risk to astronauts from exposure to radiation, for which current knowledge is

inadequate, are the biological effects and cancer risk associated with exposure to energetic high atomic number (Z) cosmic radiation (HZE). A number of laboratory-based studies have indicated that exposure to protons and other high-LET particulate radiations such as those present in galactic cosmic radiation (GCR) may change the risk to astronauts of cancer and other late health effects. Similar concerns exist for astronauts' exposure to protons from intense solar particle events (SPEs). NASA should set a high priority on continued support of research on biological markers of radiation interactions at the cellular and tissue levels. Until further information is available, NASA should continue to use current estimates of health risks associated with radiation exposures in future space missions.

- There are legal and ethical issues associated with astronauts' space missions that must be addressed by NASA in a manner beneficial to astronaut health protection. These include maintaining up-to-date policies and practices that provide acceptable limitations on radiation exposure and continued effective communication with astronauts to facilitate shared decision making on acceptable levels of risk from radiation exposures in the space environment. There also is a need to implement practices in evaluating the radiation risks of individual astronauts that are consistent with laws that protect personal information on genetic susceptibility and prior radiation exposures for medical or other purposes.

The following is a summary of recommendations based on the evaluation of genetic susceptibility and prior radiation exposures as risk factors that may contribute to overall astronaut health risks from exposure to radiation in the space environment:

- It is recommended that radiation exposure data for previous astronaut space missions be normalized to a mean daily rate (*i.e.*, mSv d^{-1}) to facilitate risk communications for future NASA space missions. Missions of different types [*e.g.*, low-Earth orbit (LEO) or deep space] and different durations (*e.g.*, days or months) should be placed into a radiation-risk perspective using these data.
- It is recommended that no genetic testing of astronauts be carried out at this time. The probability of individual astronauts having genetic susceptibility factors for radiation-induced cancer or other radiation-induced diseases is low. Furthermore, there are only a limited number of genetic

characteristics that are known today to affect the risk of radiation-induced cancers or noncancer health effects in humans.

- There is little evidence at this time that an astronaut's prior exposure to radiation, including that from medical procedures, would significantly alter the risk per unit dose associated with subsequent exposures during space exploration. It is therefore recommended that previous medical or other nonoccupational radiation exposures not be taken into account in the occupational radiation protection limitations for astronauts.
- It is recommended that NASA continue to maintain regulatory occupational dose limitations for astronauts in all types of space missions of varying durations (Tables 6.1 and 6.2). NASA should continue to use regulatory dose limits based on mainstream consensus science recommended by radiation health protection organizations, such as the National Council on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Protection (ICRP). NASA also should follow practices recommended by recognized standard-setting bodies such as the International Organization for Standardization (ISO) and the American National Standards Institute (ANSI), to establish the most defensible position from a legal perspective. NASA policies, procedures and exposure limitations used to minimize radiation risks for astronauts should consider those promulgated by various federal agencies for workers in other occupations involving radiation exposures.
- It is recommended that NASA continue to use a shared decision making model in reaching conclusions regarding appropriate levels of early and late radiation health risks associated with astronaut exposures during future space missions. NASA also should continue to provide training and maintain active discussions on radiation risk considerations with astronauts. It also is recommended that NASA maintain policies and practices that ensure the privacy of astronauts' information related to their genetic background and prior radiation exposures from medical or other sources.

1. Introduction

1.1 Purpose of the Report

This Report is an analysis of the impact of individual genetic susceptibility and previous radiation exposure on radiation-associated health risks for astronauts during and after space missions. The priority of NASA is to conduct space exploration in a safe manner. This includes selection and training of astronauts. The existence of genetic susceptibility and other diseases, and previous radiation exposures result in biological, dosimetric, legal and ethical questions that must be considered in making decisions associated with protection of present and future astronauts. This Report is organized to systematically evaluate each of these issues and provide background information that will be useful for NASA to make the necessary decisions to minimize radiation-related risks to the astronauts.

1.2 Contents of the Report

1.2.1 *Introduction*

This introduction provides a brief review of the purpose of the Report and outlines the organization of this Report in addressing NASA's concerns.

1.2.2 *Radiation Exposures Received Over Lifetimes of Astronauts*

Section 2 is directed toward briefly characterizing the space radiation environment and comparing it to medical and other radiation exposures received on Earth. Definition of the radiation environment in space is an essential part of the evaluation in this Report since astronauts will be exposed to a wide range of radiation types with different LET and energy deposition characteristics. Each of these types of radiation may have a different influence on the radiation risk associated with genetic background or previous radiation exposure.

1.2.3 *Biology Pertinent to Variations in Individual Susceptibility with Respect to Radiation Risks for Astronauts*

Section 3 reviews the information related to the influence of human genetics on radiation risk. It defines the types of health concerns from radiation, determines the baseline an individual's genetic makeup may play in modulating baseline cancer risks, and evaluates the spectrum of radiation sensitivities in the human population. The section outlines the state-of-the-field's ability to identify individual's genetic profiles that may exhibit radiation sensitivity.

1.2.4 *Predicting Cancer Risks from Previous Radiation or Chemotherapy Treatments*

The goal of Section 4 is to determine if the risk associated with previous exposures are additive to those from space flight, or if previous exposures influence the slope of the dose-response curves (*i.e.*, relationships) for subsequent exposures, thus making the combined risk higher or lower than predicted with the linear non-threshold dose-response model for ionizing radiation. This section of the Report also evaluates how medical exposures contribute to the risks for the development of cancers.

1.2.5 *Basis for Considering Medical Treatment, Disease, and Genetic Background in the NASA Occupational Radiation Protection Program*

Section 5 discusses the unique nature of the requirements for astronauts that may put them under a different set of regulatory requirements than those used for radiation workers. This is a highly-educated population that has made decisions to accept risks that are much greater than those accepted in most other professions. However, the philosophy that is used to manage radiation protection programs for radiation industry is generally applicable to the astronaut population as well.

1.2.6 *Regulatory and Statutory Issues*

If astronauts develop a disease after a space flight, there is a potential for statutory issues to arise. The decisions that NASA has to make regarding radiation protection must be framed in the current legal environment. This makes it essential to define the statutory issues associated with identifying genetically-susceptible individuals and regulating or limiting future exposures to additional radiation during space exploration. The statutory issues associated with limiting or altering the ability of an astronaut to

participate in a space mission based on either genetic background or previous radiation exposure are discussed in Section 6. In addition, there is a need for a discussion of the difficulties involved in establishing proof that adverse health effects to the astronaut, such as cancer, are due to radiation exposure while on space missions.

1.2.7 *Ethical Issues of Radiation Exposure, Genetic Background, and Astronaut Selection for Space Missions*

Biological, regulatory and legal information all contribute to the understanding of the ethical issues that must be evaluated when making decisions concerning the astronauts' radiation exposures. Ethically, NASA should provide the astronauts with sufficient information to enable astronauts to make informed choices and accept risk, while protecting individual privacy. These ethical issues are evaluated in Section 7.

1.2.8 *Background Issues, Conclusions, and Recommendations*

Background issues are reviewed including population health issues, such as the natural incidence of cancer and noncancer diseases, and background radiation exposure.

The conclusions of this Report, based on the review of normal background radiation exposures and the variable cancer rates that exist as noted in the background issues, help illustrate that it is not possible at the present time to measure an increase in cancer risk in this small population of astronauts exposed as the result of the exploration of space in LEO and the even smaller population of astronauts involved in the Apollo lunar missions beyond LEO, the only manned deep-space missions to date.

Finally, this Report provides a series of recommendations to help NASA in making difficult and important decisions related to use of information on genetic susceptibility and previous radiation exposures of the astronaut population.

These recommendations are tempered in light of the serious risks astronauts take when they embark on a space mission (*i.e.*, survivability versus the possible future risk of developing cancer later in life).

2. Radiation Exposures Received Over Lifetimes of Astronauts

Over their lifetimes, astronauts will receive a variety of radiation exposures. For any given individual, the personal radiation exposure history may be considered to begin at the point of conception. We are irradiated by natural background radiation from the moment of conception and these exposures continue throughout life. The average natural background radiation exposure to an individual in the U.S. population is $\sim 3.1 \text{ mSv y}^{-1}$ which is primarily radon exposure (NCRP, 1987a; 2009). Therefore, by the time astronauts are ready for space missions (*i.e.*, $\sim 40 \text{ y}$ of age), they have received on the order of 120 mSv from background radiation. During the course of individuals' lifetimes, other radiation exposures will occur. Examples include medical exposures and exposure during air travel. These exposures may either be nonoccupational (*e.g.*, diagnostic and therapeutic medical exposures) or occupational (*e.g.*, exposures received by nuclear power plant workers). Exposures received by astronauts in space are considered to be occupational exposures although the risks associated with radiation exposure are far below the multitude of risks inherent with the astronaut profession. Additional occupational radiation exposure will occur when flying military aircraft as a part of the requirement to maintain competence and can be documented from flight logs. Astronauts may receive additional occupational exposures in the form of medical exposures for research purposes. This section will examine the various nonoccupational and occupational exposures received by astronauts during their lifetimes. Section 2.1 reviews the relevant terminology used to quantify radiation exposures, Section 2.2 provides details regarding these various exposures, and finally Section 2.3 compares the magnitudes of the various exposures an astronaut might be expected to receive over a lifetime.

2.1 Radiation Protection Quantities

2.1.1 Absorbed Dose

Absorbed dose (D) is defined as energy deposited at a point per unit mass of *material*. SI unit for radiation absorbed dose is joule

per kilogram (J kg^{-1}), with the special name gray (Gy). The material of interest here is tissue (*i.e.*, the organs and tissues of the body), and the quantity of interest is the mean absorbed dose (D_T) in the organ or tissue (T). When evaluating stochastic effects (Section 2.1.2), D_T is the total energy deposited in the organ or tissue divided by the total mass of the organ or tissue. However, in practice, the region is defined according to the application at hand. Accordingly, organ or tissue regions that have been considered in the past range from as large as the whole body to as small as a cell nucleus or an even smaller region within a cell. The choice of organ or tissue region is dictated by a variety of factors, including: tissue regions exposed, range of radiation in tissue, and uniformity of energy deposition (NCRP, 1993a).

2.1.2 Categories of Radiation-Induced Biological Effects

For the purpose of radiation protection, radiation-induced biological effects have been categorized as either deterministic or stochastic. Deterministic effects are clinically significant biological injuries that lead to inflammatory reactions or tissue reactions that are a result of cell damage. Radiation exposures that cause deterministic effects must be above some threshold dose before a clinically significant injury can be observed. The threshold dose often depends on the dose rate. Above the threshold for a given dose rate, the extent of the injury increases with absorbed dose. An example of a deterministic effect is a radiation-related reduction in peripheral blood cells. In the past, radiation-induced cataracts in the lens of the eye were believed to have a definite threshold and were regarded as deterministic effects. However, more recent research suggests there may not be a definite threshold and the effects may be stochastic in nature (Cucinotta *et al.*, 2001a; Worgul *et al.*, 2007).

The tissues that have been of primary concern with regard to deterministic effects caused by space radiation are bone marrow and skin (NCRP, 2000a). Ovaries have been considered in discussions of potential deterministic effects in female astronauts, and it is generally believed that the typical doses received in LEO are insufficient to cause sterility (NCRP, 2000a; 2002). However, doses that are sufficiently high to cause a reduction in the number of primary oocytes, but below the threshold for causing sterility, may have some long-term impact on fertility. Such a reduction in primary oocytes, which are irreplaceable, would be categorized as a deterministic effect. Consideration of medical exposures received by astronauts, particularly those of a therapeutic nature, substantially broadens their number of tissues at potential risk for deterministic effects. Therapeutic uses of ionizing radiation deliver the

highest human tissue doses. Lengthy fluoroscopically-guided interventional medical procedures can also lead to deterministic effects. While the underlying health problems associated with such procedures likely would disqualify an individual from being accepted into the astronaut training program, the impact of such exposures on radiation risk-estimates and consequent flight status of matriculated astronauts is of importance to this Report. Other diagnostic uses of ionizing radiation generally deliver doses well below values that cause deterministic effects.

Stochastic effects are defined as biological consequences whose probability of occurrence increases with absorbed dose. However, the severity of the biological effects do not depend on dose. It is generally considered that there is no threshold dose required to cause stochastic effects. Cancer and heritable effects are considered to be stochastic effects. For radiation protection purposes, it has generally been assumed that the probability of stochastic effects increases linearly with absorbed dose (NA/NRC, 2006; NCRP, 2001a), although experimental observations such as bystander effects and adaptive responses are fostering debate over this assumption (de Toledo and Azzam, 2006). This is an ongoing research area and the relevance of these effects in animal models and cell culture to human exposure is unclear (Groesser *et al.*, 2008; Hei *et al.*, 2008; Sowa *et al.*, 2010). An epidemiological study published on the United Kingdom Registry of Radiation Workers found that the results were consistent with linear nonthreshold (Muirhead *et al.*, 2009).

2.1.3 Radiation Protection Quantities for Deterministic Effects

NCRP (2002) and subsequent NCRP reports express the dose limits for astronauts concerning deterministic effects in terms of a quantity named gray equivalent (G_T), with the name for its unit also named gray equivalent (Gy-Eq). It is recognized that the use of the gray equivalent poses problems with respect to the SI system of units. According to the requirements of the SI system of units, the gray equivalent should neither be used as a named quantity nor a unit. Neither the gray equivalent (G_T) nor the name for its unit (Gy-Eq) used by NCRP for radiation protection purposes for deterministic effects are used universally. For such an application, ICRP (2007) recommends using the quantity relative biological effectiveness (RBE) weighted absorbed dose expressed in gray.

The gray equivalent is the mean absorbed dose in the tissue modified by a factor to account for the RBE of the specified radiation for causing deterministic effects. For deterministic effects, this factor is denoted by R_i . Thus, the gray equivalent for tissue T is:

$$G_T = \sum_i R_i D_{T,i}, \quad (2.1)$$

where R_i is the RBE for deterministic effects caused by the i th radiation type, and $D_{T,i}$ is the mean absorbed dose to tissue T from the i th radiation type. The special named unit of the gray equivalent is Gy-Eq (ICRP, 2003; NCRP, 2002). Table 2.1 gives the recommended values of R_i for neutrons, heavy ions, protons, electrons and positrons, and photons.

The values for neutrons, heavy ions, and protons are taken from NCRP Report No. 132 (NCRP, 2000a) which in turn were adapted from ICRP Publication 58 (ICRP, 1989). Accordingly, for the purposes of this Report, the R_i values for electrons, positrons and photons also have been adapted from ICRP Publication 58 (ICRP, 1989).

2.1.4 Radiation Protection Quantities for Stochastic Effects

Dose limits for stochastic effects have been defined by NCRP in terms of the equivalent dose and effective dose (NCRP, 1993b). Equivalent dose is the mean absorbed dose in an organ or tissue modified by a factor to account for the RBE of the specified radiation for stochastic effects. This factor, originally defined by ICRP (1991a) is denoted the radiation weighting factor (w_R). Table 2.2 lists w_R for different types of radiation R using the updated values in ICRP Publication 103 (ICRP, 2007).

TABLE 2.1—*Relative biological effectiveness (R_i) for deterministic effects for use in converting D_T to G_T .*

Particle Type	R_i (range for value) ^a	Reference
1 – 5 MeV neutrons	6.0 (4 – 8)	NCRP (2000a)
5 – 50 MeV neutrons	3.5 (2 – 5)	NCRP (2000a)
Heavy ions (<i>e.g.</i> , helium, carbon, neon, argon)	2.5 (1 – 4)	NCRP (2000a)
Protons >2 MeV	1.5	NCRP (2000a)
Electrons, positrons	1	ICRP (1989)
Photons (all energies of x and gamma rays)	1	ICRP (1989)

^aThe R_i values adapted from ICRP Publication 58 (ICRP, 1989) are for fractionated exposures of 2 to 3 Gy per fraction. These dose fractions are significantly greater than the mission doses anticipated in most NASA astronaut missions.

TABLE 2.2—*Radiation weighting factors (w_R) for converting D_T to H_T for stochastic effects.^a*

Particle Type ^b	w_R
Neutrons, $E_n < 1$ MeV	$2.5 + 18.2 e^{-\frac{[\ln(E_n)]^2}{6}}$
Neutrons, $1 \text{ MeV} \leq E_n \leq 50 \text{ MeV}$	$5.0 + 17.0 e^{-\frac{[\ln(E_n)]^2}{6}}$
Neutrons, $E_n > 50 \text{ MeV}$	$2.5 + 3.25 e^{-\frac{[\ln(0.04E_n)]^2}{6}}$
Alpha particles, fission fragments, alpha recoil nuclei, and nonrelativistic heavy ions	20
Protons, other than recoil protons, energy $>2 \text{ MeV}$	2
Electrons, positrons and muons, all energies	1
Photons (all energies of x and gamma rays)	1

^aAdapted from ICRP (2007).^b E_n is neutron energy in million electron volts (e.g., for 50 keV neutrons $E_n = 0.05 \text{ MeV}$).

ICRP defines the equivalent dose to be used exclusively for stochastic effects (ICRP, 1991a; 2007). Thus, the equivalent dose H_T to tissue T is:

$$H_T = \sum_R w_R D_{T,R}, \quad (2.2)$$

here the summation is over the R radiation types. The SI unit for equivalent dose is J kg^{-1} with the special name sievert (Sv).

Effective dose (E) is defined as:

$$E = \sum_T w_T H_T, \quad (2.3)$$

where w_T is the tissue weighting factor. The w_T take into account the relative radiosensitivity of the tissues. Values of w_T were originally

assigned in ICRP Publication 60 (ICRP, 1991a), and subsequently adopted by the NCRP (2000a). Table 2.3 gives the revised values that now appear in ICRP Publication 103 (ICRP, 2007). The unit of effective dose is also J kg^{-1} (with the special name sievert).

ICRP (1991a; 2007) is the general approach for radiation protection purposes. Radiation protection considerations are complex for astronauts exposed to the mixtures of high- and low-LET radiations in space. NCRP has adopted an approach that obtains point values of absorbed dose (D) and dose equivalent (H) in the organ or tissue, where $H = DQ$ and Q is the quality factor. There is some experimental evidence to suggest that the w_R value of 20 for heavy ions may represent an overestimate of the mutagenic and carcinogenic effects of these radiations. The slopes of dose response curves for induction of chromosomal instability by HZE particles are not as steep as those for alpha particles for cellular effects (Limoli *et al.*, 2000). Because of this, NASA uses variable quality factors. Using quality factor relationships as a function of LET [$Q(L)$], the quantity organ dose equivalent is obtained by integrating over L and averaging the point values (ICRP, 1998; NCRP, 2002). The organ dose equivalent is then used as an acceptable approximation for H_T in the effective dose formulation.

Finally, it should be noted that the effective dose formalism is only an approximate surrogate for risk in cases of partial-body exposures (*e.g.*, x rays, radioactive compounds in the body). As acknowledged by ICRP, effective dose is intended to be used as a radiation protection quantity only, and its use in retrospective assessments of risk from actual exposures often is not appropriate. In medicine, the effective dose can have misleading implications.

TABLE 2.3—*Recommended w_T* ^a

Tissue or Organ	w_T
Bone marrow (red), colon, lung, stomach, breast, and remainder tissues ^b	0.12
Gonads	0.08
Bladder, esophagus, liver, and thyroid	0.04
Bone surface, brain, salivary glands, and skin	0.01

^aAdopted from ICRP (2007).

^bTissues included in the remainder are: adrenals, extrathoracic region, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate (for males), small intestine, spleen, thymus, and uterus/cervix (for females).

For example, treatment or diagnostic procedures using radioactive iodine could give a meaningful dose to the thyroid but the effective dose might look insignificant. Thus, in terms of risk for partial-body exposure of individuals, it is important to use the radiation absorbed dose to the organ exposed along with the appropriate RBE values.

2.2 Sources of Exposure to Ionizing Radiation

2.2.1 *Radiation Exposures Received by the U.S. Population*

Exposure to natural background radiation is a part of our daily existence. The annual background radiation exposure incurred by the U.S. population arises from a variety of sources including cosmic rays, cosmogenic radionuclides (*e.g.*, ^3H , ^{14}C , ^7Be), radionuclides in the body (*e.g.*, ^{40}K), terrestrial radiation (*e.g.*, uranium), and inhaled radionuclides (*e.g.*, ^{222}Rn). The average annual effective dose from all natural sources to an individual in the U.S. population is ~ 3.1 mSv (NCRP, 1987a; 2009). However, natural background exposures received by any given individual vary across the United States depending on geographic location and presence of radon in the home as noted in NCRP Report No. 160 (NCRP, 2009).

Additional exposures above natural background are incurred from man-made sources which comprise a value of ~ 0.6 mSv y^{-1} per individual in the U.S. population according to a report based on data from the early 1980s (NCRP, 1987b). Recent estimates by NCRP (2009) indicate that the value for man-made sources for 2006 has increased to ~ 3.1 mSv y^{-1} . Man-made exposures arise from radiation emitted by medical procedures, consumer products such as smoke detectors, and occupational exposures. The largest man-made contribution is medical exposures (*i.e.*, exposures received by patients during diagnostic and interventional procedures that use ionizing radiation). Therapeutic exposures are not included in this estimate because the concept of effective dose may not be applicable to this source of exposure (NCRP, 2009). Based on recent estimates by NCRP (2009), exposures from medical procedures increased from the previous value of 0.5 mSv y^{-1} for the early 1980s (NCRP, 1987b) to 3 mSv y^{-1} for 2006, primarily due to increased utilization of diagnostic and interventional medical procedures. It should be kept in mind that the value of 3 mSv y^{-1} for medical exposures is averaged over all individuals in the U.S. population (whether actually exposed or not). The exposures received by a given individual in the population may vary greatly from this value in either direction (*e.g.*, a person that requires several diagnostic or interventional medical procedures in a given year for health care may far exceed the average value).

The average exposure to the entire U.S. population from occupational exposures is a small fraction of the total annual average exposure (for 2006, the value was $<0.1 \text{ mSv y}^{-1}$) (NCRP, 2009). However, individuals that are occupationally exposed (but not including astronauts) receive an average value of 1.1 mSv y^{-1} (NCRP, 2009). Airline flight crews accrue higher values, the average is $\sim 3.1 \text{ mSv y}^{-1}$ (NCRP, 2009). Astronauts receive occupational radiation exposures but they are a small minority of the cohort of occupationally exposed workers and their exposures are considered separately. Astronauts generally receive $\sim 1 \text{ mSv d}^{-1}$ in space (Reitz *et al.*, 2009), however there have been no significant SPEs (Section 2.2.3.1) for any space missions in LEO to date (NCRP, 2002). U.S. federal laws mandate that occupational whole-body exposures be kept below 50 mSv y^{-1} (NRC, 2008). While there is a distribution of values for those occupationally exposed, few individuals receive exposures at the higher levels (NCRP, 2009). There is a mechanism by which occupationally exposed individuals can receive additional doses that are accounted for separately from the doses received under the limits specified in 10 CFR Part 20.1201 (NRC, 2008). These are called “planned special exposures” and they are allowed only in exceptional situations when alternatives are unavailable or impractical (NRC, 2008).

A given astronaut’s ionizing radiation exposure history will come from a number of sources including (but not limited to): natural background, medical procedures and other man-made sources, jet aircraft flight, and space flight. In the sections that follow, the magnitudes of these various exposure scenarios are examined and compared.

2.2.2 Medical Exposures

Astronauts may undergo a variety of exposures to ionizing radiation as a consequence of diagnostic and therapeutic procedures that may be received during routine physical examinations and medical interventions. Astronauts also may receive medical exposures prior to becoming an astronaut and may have medical exposures to ionizing radiation during the years after completing their NASA service. The nature of the exposures can vary considerably with respect to radiation type, dose, dose rate, and number of exposures. Additionally, the volume of tissue irradiated and the uniformity of the dose delivered to the tissue can vary considerably. The irradiated tissue volumes range from whole body to organ, tissue, and even cell. These variables will be discussed in the context of the various diagnostic and therapeutic procedures that astronauts may receive in the course of medical care.

2.2.2.1 Diagnostic Medical Exposures. Diagnostic medical exposures to ionizing radiation can be broadly grouped into several categories that differ substantially with regard to type and source of radiation, dose, dose rate, and the tissues that are irradiated. These broad categories include projection imaging, fluoroscopy, computed tomography (CT), and nuclear medicine. The former three categories utilize x-ray beams that enter one side of the body and emerge from the opposing side of the body to produce images that represent anatomical and functional (*e.g.*, fluoroscopy) features within the body. In contrast, nuclear medicine imaging relies on capturing radiation that emanates from the body after administering radioactive pharmaceuticals (*i.e.*, radiopharmaceuticals) to the patient. By virtue of the ionizing radiations used to produce the various images captured in diagnostic radiology, each procedure results in some degree of radiation exposure of the patient. The volume of tissue irradiated and absorbed doses delivered by procedures vary considerably with the lowest doses typically delivered by projection techniques (*e.g.*, chest x rays) and the higher doses delivered by diagnostic procedures that use fluoroscopy. Dose rates delivered by the various procedures can vary by several orders of magnitude even for diagnostic studies. The radiation exposures associated with a number of procedures used in diagnostic radiology are outlined below.

In the United States (NCRP, 2009), ~11 % of medical exposures involved conventional x-ray projection imaging (*e.g.*, chest x rays and mammography) and fluoroscopy. Table 2.4 gives the absorbed doses and effective doses associated with several common diagnostic x-ray procedures.

With the advent of high throughput technology, CT is capturing an ever increasing share of diagnostic imaging. While CT constituted only a couple of percent of all diagnostic radiology procedures a decade ago, current trends indicate that CT now comprises ~17 % of all diagnostic procedures in a U.S. radiology department with a typical referral pattern (NCRP, 2009). Table 2.5 provides typical absorbed doses and effective doses for a number of common CT procedures. Even more significant is the trend toward increasing absorbed doses and the volume of tissue irradiated. This has arisen because multidetector CT technology is now widely used to provide rapid detailed images of body regions (*e.g.*, head or abdomen) or combination of regions (*e.g.*, head, cervical spine, abdomen, and pelvis) in a matter of seconds (NCRP, 2009). These techniques deliver skin doses up to 20 to 70 mGy and exposed organs receive doses about half those values (Nickoloff and Alderson, 2001). These x rays also are assigned a w_R of unity [*i.e.*, absorbed dose (milligray) and equivalent dose (millisievert) are numerically the same].

TABLE 2.4—Typical absorbed doses and effective doses to patients from common diagnostic x-ray procedures.^a

Examination	Active Marrow (mGy)	Thyroid (mGy)	Breast (mGy)	Uterus (mGy)	Ovaries (mGy)	Testes (mGy)	Effective Dose ^b (mSv)
Chest	0.04	0.02	0.09	— ^c	— ^c	— ^c	0.04
Skull	0.2	0.4	— ^c	0.06	— ^c	— ^c	0.1
Abdomen	0.4	— ^c	0.03	2.9	2.2	0.4	1.2
Thoracic spine	0.7	1.5	1.3	— ^c	— ^c	— ^c	1.0
Lumbar spine	1.4	— ^c	0.07	3.5	4.3	0.06	2.1
Pelvis	0.2	— ^c	— ^c	1.7	1.2	4.6	1.1
Intravenous urography	1.9	0.4	3.9	3.6	3.6	4.3	4.2
Barium enema (including fluoro)	8.2	0.2	0.7	16	16	3.4	8.7
Mammography (film-screen)	— ^c	— ^c	2	— ^c	— ^c	— ^c	0.1

^aTable adapted from Bushberg *et al.* (2002).^bAdditional information on effective doses for diagnostic procedures can be found in NCRP (2009).^cValues are <0.01 mGy.

TABLE 2.5—*Typical radiation absorbed doses ($CTDI_{vol}$)^a and effective dose to adults from CT.^b*

CT Examination	$CTDI_{vol}$ (mGy)	Effective Dose ^c (mSv)
Head	65	1.5
Chest	8.9	5.8
Abdomen	12	5.3
Abdomen and pelvis	11	7.1

^a $CTDI_{vol}$ = volume weighted CT dose index.^bTable adapted from Shrimpton *et al.* (2006). Values represent the mean of slice Classes 1, 2, 4, and 8+.^cAdditional information on effective doses for CT procedures can be found in NCRP (2009).

Diagnostic nuclear medicine procedures involve the administration of radiopharmaceuticals to patients to gain information regarding physiological function of organs and tissues. Radiopharmaceuticals are prepared with a number of different radionuclides such as: ^{67}Ga , $^{99\text{m}}\text{Tc}$, ^{111}In , ^{123}I , ^{131}I , ^{133}Xe , and ^{201}Tl . The radiopharmaceuticals are administered by a variety of pathways (*i.e.*, generally by intravenous, airway or oral routes). Radiopharmaceuticals are selected based on their capacity to be selectively retained in various tissues in the body. Upon localization of the radiopharmaceutical in the organ or tissue to be imaged, x or gamma rays emitted by the radionuclides are captured and used to form images containing useful diagnostic information. Each radiopharmaceutical has a unique pattern of biological uptake and clearance in each organ and tissue of the body. Consequently, these agents generally are distributed nonuniformly throughout the body. Differences in the uptake of activity occur over a variety of spatial dimensions ranging from organs to cells. Furthermore, each radionuclide has a unique physical half-life and a unique set of radiations that it emits upon decay. Accordingly, tissues and cells within the body can receive a wide range of absorbed doses that are typically delivered over minutes to days depending on the biological uptake and clearance in the tissue and the physical half-life of the radionuclide. These aspects are discussed in detail in ICRU Report 67 (ICRU, 2002). A compendium of dosimetry reports can be found in ICRP Publication 53 (ICRP, 1987) with updates in ICRP Publication 62 (ICRP, 1991b), ICRP Publication 80 (ICRP, 1998), and ICRP Publication 106 (ICRP, 2008).

Table 2.6 lists the mean absorbed doses to organs and tissues and effective dose per unit of administered activity for a few common radiopharmaceuticals. The SI unit of administered activity is disintegration per second with the special name becquerel (Bq) (*i.e.*, 1 Bq = 1 dps). The amount of administered activity varies. Table 2.7 gives the administered activities of ^{99m}Tc -pertechnetate and Na^{131}I along with the corresponding mean absorbed doses to several organs. The cardiac imaging agent $^{201}\text{TlCl}$ is included as an example of a diagnostic radiopharmaceutical that may be used in the event of a suspected cardiac condition. Regardless of whether positive or negative diagnostic findings result, the individual will have been exposed as indicated in Tables 2.6 and 2.7. Although only ~5 % of medical procedures are diagnostic nuclear medicine procedures, 26 % of the dose to individuals in the U.S. population from medical procedures is attributed to nuclear medicine studies (NCRP, 2009). Furthermore, 85 % of the dose from nuclear medicine is from cardiac studies (NCRP, 2009).

As noted above, the values quoted in Tables 2.6 and 2.7 are estimates of mean absorbed doses to organs and tissues. The absorbed dose to individual cells within the organ or tissue may be orders of magnitude higher or lower than the mean depending on the radiopharmaceutical, its microscopic distribution within the organ or tissue, and its subcellular distribution (ICRU, 2002). The RBE of the radiations emitted by these radionuclides can be high depending on the subcellular distribution of the radionuclide. While this phenomenon is well known for radiopharmaceuticals that emit very low energy Auger electrons (*e.g.*, ^{125}I , ^{111}In , ^{201}Tl) (Humm *et al.*, 1994), subcellular distribution also has been shown to play a role in the radiotoxicity of ^{131}I (Neti and Howell, 2004). Furthermore, the absorbed doses from these radiopharmaceuticals are chronically delivered with dose rates that vary exponentially in time and that extend over minutes to hours to days. For example, the physical half-life for radioactive ^{131}I is ~8 d and, following its accumulation in the thyroid, there is minimal biological clearance from this organ. Therefore, its retention time in the thyroid can be several months, during which it delivers low-dose rate chronic exposure to the thyroid. Hence, there are some similarities between radiation exposures encountered in space flight and nuclear medicine.

2.2.2.2 Interventional Medical Exposures. Fluoroscopic procedures are used extensively in the practice of medicine. Most conventional diagnostic fluoroscopic procedures deliver relatively low absorbed doses to the patient while interventional fluoroscopic procedures can lead to very high doses being delivered. Generally, the skin

TABLE 2.6—Mean absorbed doses to organs and tissues ($mGy MBq^{-1}$) and effective doses ($mSv MBq^{-1}$) from diagnostic nuclear medicine studies in adults.^{a,b}

Organ	$^{201}TlCl$ ^b	$Na^{131}I$ ^{a,c}	^{99m}Tc -pertechnetate ^b
Adrenals	0.057	0.046	0.0037
Bladder	0.040	0.34	0.018
Bone surfaces	0.34	0.091	0.0054
Brain	0.022	NA ^d	0.0020
Breast	0.024	0.079	0.0018
Gall bladder	0.065	NA ^d	0.0074
GI tract			
Stomach wall	0.099	0.46	0.026
Small intestine	0.14	0.28	0.016
Colon	0.23	NA ^d	0.042
Upper large intestine	0.17	0.059	0.057
Lower large intestine	0.32	0.04	0.021
Heart	0.20	NA ^d	0.0031
Kidneys	0.48	0.053	0.0050
Liver	0.15	0.040	0.0038
Lungs	0.11	0.11	0.0026

Muscle	0.052	NA ^d	0.0032
Esophagus	0.036	NA ^d	0.0024
Ovaries	0.73	0.042	0.010
Pancreas	0.057	0.056	0.0056
Red bone marrow	0.16	0.10	0.0036
Skin	0.022	NA ^d	0.0018
Spleen	0.12	0.049	0.0043
Testes	0.45	0.026	0.0028
Thymus	0.036	NA ^d	0.0024
Thyroid	0.22	640	0.022
Uterus	0.051	0.048	0.0081
Remaining organs	0.058	0.14	0.0035
Effective dose (mSv MBq ⁻¹) ^e	0.22	19	0.013

^aICRP Publication 53 (ICRP, 1987).^bICRP Publication 80 (ICRP, 1998).^cAssumes 45 % of injected activity is taken up by the thyroid.^dNot available.^eAdditional information on effective doses for nuclear medicine procedures can be found in NCRP (2009).

TABLE 2.7—*Typical mean absorbed doses to organs and tissues from selected nuclear medicine procedures*
(NCRP, 1987a; 1998).

Radiopharmaceutical	Administered Activity (MBq)	D_T Thyroid (mGy)	D_T Ovaries (mGy)	D_T Testes (mGy)	D_T Marrow (mGy)	Effective Dose ^a (mSv)
^{99m} Tc-pertechnetate	740 ^b	17	7.4	2.1	2.7	9.6
Na ¹³¹ I	3.7 ^c	2,370	0.16	0.096	0.37	70
²⁰¹ TlCl	150 ^d	110	110	68	24	33

^aAdditional information on effective doses for nuclear medicine procedures can be found in NCRP (2009).

^bMedi-Physics, Inc., Amersham Healthcare.

^cDRAXIMAGE, a division of DRAXIS Specialty Pharmaceuticals, Inc.

^dMallinckrodt, Inc.

where the x rays enter the body (*i.e.*, local tissue) receives the highest doses in fluoroscopic procedures. However, tissues within the body also are similarly exposed. As an example, Table 2.8 gives typical skin doses delivered during coronary angiography and several interventional fluoroscopic procedures. The skin doses delivered by these fluoroscopic procedures vary considerably depending on many variables such as:

- patient size;
- medical complications;
- skill of the fluoroscopist; and
- complexity of the procedure.

These factors also affect the time over which the tissues are irradiated. However, generally, fluoroscopy involves sporadic exposures from 20 to $>50 \text{ mGy min}^{-1}$ (NCRP, 2009). Based on Table 2.8, irradiation times range from a minute to more than an hour. It should be noted that while the clinical findings of interventional procedures may disqualify an astronaut from further missions based on medical considerations, coronary angiography studies with negative findings, for example, may not. However, if flight certification considers both nonoccupational and occupational exposures, the radiation exposures resulting from negative findings could potentially disqualify astronauts from further space missions.

TABLE 2.8—*Typical local skin absorbed doses from interventional fluoroscopic procedures.*

Procedures	Skin Absorbed Dose (mGy)
Coronary angiography (CA)	1,250 ^a
Interventional without CA (I)	3,600 ^a
Interventional with CA (I + CA)	3,300 ^a
RF ablation for cardiac dysrhythmias	1,500 – 1,800 ^b
Neuroembolization (head)	2,000 ^c
Neuroembolization (spine)	3,700 ^c
TIPS creation ^d	2,200 ^c

^aAdapted from ICRP Publication 85 (ICRP, 2000).

^bPadovani and Quai (2005).

^cMiller *et al.* (2003); values rounded off to the nearest hundredth.

^dTIPS = transjugular intrahepatic portosystemic shunt.

2.2.2.3 Therapeutic Medical Exposures. Therapeutic use of ionizing radiation necessarily involves irradiation of target tissues with very high doses. Radiation therapy modalities use a variety of sources of ionizing radiation. Most common are external beams of megavoltage x rays and electrons. However, among the other sources are proton beams, neutron beams, and gamma rays from sealed “seeds” containing radionuclides. Radiation oncology procedures generally deliver tens of gray to the tumor and much lower, although often substantial, doses to presumably healthy tissues. Therapeutic medical exposures may be delivered over time in fractions at relatively high-dose rates or over longer periods of time at lower dose rates. For example, a typical fractionated radiation therapy schedule may involve daily exposures of ~2 Gy for 5 d a week for six weeks.

Radiation therapy also is delivered using nuclear medicine radiopharmaceuticals. Treatment of Grave’s disease and thyroid carcinoma are the most common therapeutic procedures in nuclear medicine. Thyroid carcinoma is commonly treated with Na^{131}I . The administered activity generally varies from patient to patient with a range of 1.85 to 7.4 GBq (Parthasarathy and Crawford, 2002). Using the information provided in Table 2.7, and assuming an administered activity of 5 GBq, this therapy will deliver a red bone marrow dose of ~0.5 Gy.

2.2.2.4 Dependence of Photon RBE on Energy. It should be noted that, although w_R has been set to unity for all ionizing photons (*i.e.*, $w_R = 1$, Table 2.1), there are experimental data that show that photon RBE values can have a substantial dependence on energy (ICRP, 2003; NA/NRC, 2006). Diagnostic and therapeutic medical exposures generally include a very broad range of photon energies. The highest photon energies used in medical exposures are produced by megavoltage linear accelerators used in radiation oncology. These generate x rays with energies as high as 25 MeV. At the other end of the spectrum, the lowest photon energies used in medical exposures are characteristic x rays emitted by nuclear medicine radionuclides that decay by electron capture or internal conversion. Similar energies are emitted by mammographic x-ray tubes that are generally operated at 20 to 30 kVp. When combined with filtration, these generate low-energy photons predominately in the range of 10 to 30 keV. When compared to 220 kVp x rays, RBE values as high as three have been reported for cell transformations induced by mammographic x rays (Frankenberg *et al.*, 2002; Goggelmann *et al.*, 2003). Even higher RBE values have been reported when ^{60}Co gamma rays were used as the reference radiation (Schmid, 2002). Therefore, when considering the radiogenic

cancer risk of exposure to nuclear medicine radiopharmaceuticals, medical x rays and CT scans, it is important to be aware that RBE for exposure to low-energy photons may be higher (by factors of two or three) compared to exposure to high-energy gamma rays under similar conditions (Fayard *et al.*, 2002; Hill, 2004; Hill *et al.*, 2006; Kocher *et al.*, 2005; Trabalka and Kocher, 2007).

2.2.3 *Space Radiation Exposures During Previous Space Missions*

2.2.3.1 *Space Radiations in Low-Earth Orbit.* As detailed by Badhwar (1997) and in an earlier NCRP (2000a) report, there are three general types of space radiation in LEO. These are:

- trapped particle radiation;
- galactic cosmic radiation (GCR); and
- solar particle radiation.

Trapped particle radiation consists of protons, electrons, and a small component of heavy ions, all of which are trapped in closed orbits (belts) by Earth's magnetic field. The flux of the various particles depends on solar activity. Protons contribute the highest absorbed dose in the inner belt. A continuous distribution of proton energies is present with the proton energy range dependent on the distance from Earth. In this context, distances from Earth usually are given in terms of the mean radius of Earth [6,371 km (R_E)]. Peak fluence rates occur at 1.3, 2 and 3 R_E for 400, 4, and 0.3 MeV protons, respectively. The outer belt consists principally of electrons. The trapped electrons in the inner and outer belts are separated by a "slot" at 2.8 R_E . Like protons, a spectrum of electron energies is present with a range from 0 to ~6 MeV at an altitude of 400 km. Details regarding trapped particle radiations were provided in NCRP Report No. 132 (NCRP, 2000a).

GCR is made up of high-energy protons, some helium ions, and much smaller numbers of heavy ions that include all of the naturally occurring elements. Those of dosimetric importance include hydrogen, helium, carbon, oxygen, neon, silicon, and iron nuclei. The source of these ions is outside of our solar system. GCRs have energies ranging from a few MeV n^{-1} up to 10^{15} MeV n^{-1} . The flux of GCRs also is influenced by solar activity with it being lowest during solar maximums and highest during solar minimums, which are described in detail in NCRP Report No. 132 (NCRP, 2000a).

SPEs are believed to arise from both solar flares and the acceleration associated with interplanetary shocks generated by fast coronal mass ejections. Solar particle radiation has a similar

composition to GCR (*i.e.*, protons, helium and heavier ions), but originates from the sun. Protons constitute the majority of SPE ions, with fluences per SPE reaching levels $>10^{10}$ protons cm^{-2} with energies >10 MeV. These high fluences can last up to several days. The energies of helium ions and the heavy ions are generally <20 MeV n^{-1} ; however, these are not prevalent and generally are considered to be negligible from a dosimetric standpoint (NCRP, 2000a).

2.2.3.2 Space Radiation Dose Rates in Low-Earth Orbit. The dose rate of space radiation depends on a number of variables (NCRP, 1989; 2000a). Close to Earth where the space radiation environment is affected strongly by Earth's magnetic field, Earth's atmosphere, and the sun, the radiation dose rate depends on:

- altitude
- latitude
- longitude
- solar activity

In general, the dose rate increases with increasing altitude due to the decreasing thickness of the atmosphere with altitude, Figures 2.5 and 2.6 in NCRP Report No. 94 (NCRP, 1987b). The dose rate increases with increasing latitude with the dose rate being the highest over the North and South Poles. Outside of Earth's atmosphere, there is an inner and an outer trapped radiation belt. The inner belt, called the Van Allen belt in honor of its discoverer, is made up primarily of protons (some individuals refer to both the proton belt and the electron belt as Van Allen belts). The proton belt dips closest to Earth, within 500 km, at approximately -30 degrees latitude and -45 degrees longitude in an area off the Eastern coast of Brazil called the South Atlantic Anomaly (SAA). SAA is due to an anomaly in Earth's magnetic field. The flux of protons in SAA, with energies above 50 MeV, is increased $\sim 1,000$ times relative to the proton flux at the same altitude outside SAA. The proton belt extends out to $\sim 1 R_E$ (*i.e.*, 6,371 km). The outer belt consists primarily of electrons and is divided into an inner electron zone and an outer electron zone. The inner electron zone extends out to $\sim 2.8 R_E$ while the outer electron zone is from ~ 2.8 to $\sim 12 R_E$ (NCRP, 1989). The dose rate in the outer electron zone is ~ 10 times greater than in the inner electron zone (NCRP, 1989).

At distances from Earth where the effect of Earth's magnetic field is small, the dose rate depends on the GCR background and the sun's solar activity and associated magnetic fields. The dose rate from GCR is relatively constant. The dose rate from "normal"

solar activity in space (beyond the influence of Earth) varies during the ~11 y solar cycle, being higher at solar minimums than at solar maximums due to the greater shielding effects of the sun's magnetic field during solar maximums. Beyond the direct effects of the sun's magnetic field and the radiation of SPEs, the dose rate in "free space" is $\sim 0.35 \text{ Sv y}^{-1}$ (NCRP, 2006a). SPEs can cause the dose rate to change dramatically, resulting in unshielded dose rates of tenths of sievert per hour for periods of several hours to days, at locations not shielded by Earth's atmosphere and/or Earth's magnetic field (NCRP, 2002).

2.2.3.3 Astronauts' Exposures in Skylab. Skylab was placed into a 435 km circular orbit at an inclination with Earth's equator of 50 degrees in July of 1972 and was subsequently visited by three groups of astronauts identified as Skylab Missions 2, 3 and 4. The mean doses to the crew members ranged from 20 to 80 mGy. These values and corresponding dose equivalents to selected tissues are given in Table 2.9.

2.2.3.4 Space Transportation System Exposures. Table 2.10 gives the whole-body dose equivalent measured by space transportation system (STS), better known publicly as the space shuttle, passive dosimetry in orbits differing in inclination and altitude. It is apparent that the dose equivalent rate increases with both inclination and altitude. The dose equivalent rate can vary from $<0.1 \text{ mSv d}^{-1}$ up to nearly 1 mSv d^{-1} .

2.2.3.5 Astronauts' Exposures in Mir and International Space Stations. The Mir Space Station orbited in a slightly elliptical orbit

TABLE 2.9—*Skylab crew member exposures.*^a

Skylab Mission	Duration ^b (d)	Mean Dose ^c (mGy)	Skin ^d (mSv)	Lens ^d (mSv)	BFO ^{d,b} (mSv)
2	28	20	37	26	16
3	59	47	74	59	36
4	84	78	140	130	79

^aValues adapted from Table 9-IV in Bailey *et al.* (1977) and rounded to two significant figures.

^bBFO = blood forming organs.

^cMean doses from personal radiation dosimeters placed at four locations.

^dDose equivalent calculated assuming $Q_{\text{proton}} = 1.5$ for eye and skin, and $Q_{\text{proton}} = 1.6$ for BFO. Electron dose applied to skin only with $Q_{\text{electron}} = 1$. Only values for the commander are given.

TABLE 2.10—*Dose equivalent to the whole body in the space shuttle (NCRP, 1989).*

Shuttle Mission	Inclination (degrees)	Altitude (km)	Duration (d)	Dose Equivalent (mSv)	Dose Equivalent Rate (mSv d ⁻¹)
STS-3	40.3	280	8.1	0.685	0.085
STS-4	28.5	297	7.04	0.679	0.096
STS-9	57	241	10	1.797	0.1797
STS-41C	28.5	519	7	5.04	0.72

with a mean altitude of 400 km and a high inclination with respect to Earth's equator of 51.6 degrees. A sampling of daily dose rates for the Mir Space Station is given in Table 2.11. The International Space Station (ISS) is designed for an operating altitude of 360 to 450 km and an inclination of 51.6 degrees. A sampling of daily dose rates for ISS also is given in Table 2.11 along with totals for 180 d missions on ISS and Mir.

2.2.3.6 Astronauts' Exposures Beyond Low-Earth Orbit. The only astronauts to have crewed space missions beyond LEO were those who flew the Apollo lunar flights. Those astronauts acquired doses over the course of the few days of their missions that were comparable to total doses on longer STS missions (Figure 2.1). Because of the lack of data on space missions outside of LEO, NCRP (2006a) has noted that additional information is needed to ensure adequate information is available for making radiation protection recommendations. Longer deep-space missions, such as a Mars mission (Cucinotta *et al.*, 2001b), will require months to years for completion, with deep-space travel lasting up to six months each way. During such longer periods in space beyond Earth's magnetic fields, the greatest concern would be exposures to significant SPEs. There have been recorded instances of SPE events that could have led to onset of the prodromal radiation syndrome for astronauts had a crew been in space during those events, but would not have resulted in lethality (NCRP, 2006a). These issues apply to lunar base missions as well, which along with the Mars missions are the only astronaut-crewed deep-space missions currently under consideration by NASA. It is recognized that typical SPEs are not a great concern to NASA and that for these deep-space missions GCR radiation would be of more concern.

TABLE 2.11—*Dose equivalent during Mir and ISS missions*
(Wilson, 2000).

Mission	Trapped (mSv d ⁻¹)	GCR (mSv d ⁻¹)	Total (mSv d ⁻¹)	Estimate for 180 d Mission (mSv)
Mir	0.538	0.445	1.003	181
ISS	0.33	0.28	0.61	110

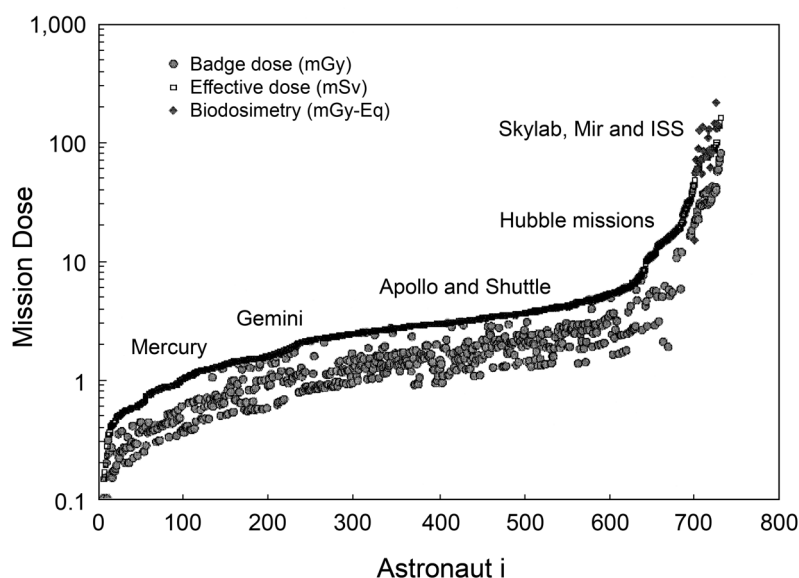


Fig. 2.1. Summary of mission badge dose, effective dose and population average biological dose equivalent for astronauts on all NASA space missions including: Mercury, Gemini, Apollo, Skylab, Apollo-Soyuz, Shuttle (STS), NASA-Mir, and ISS missions (adapted from Cucinotta *et al.*, 2008). The open squares can be seen in both the upper right and lower left portions of the figure. The high density of open squares results in what appear to be closed black symbols. The coordinates x and y equal Astronaut Index and Mission Dose, respectively, and have been sorted in order of ascending mission dose for clarity, not necessarily time order. There is a correlation as missions have increased in duration over time.

2.2.3.7 Biodosimetry and Comparison of Astronauts' Exposures in Space. The doses received by all astronauts during all classes of NASA missions have been compared by Cucinotta *et al.* (2008) as shown in Figure 2.1. Based on thermoluminescent dosimeter (TLD) doses recorded early in the NASA space program, astronauts on the Mercury and Gemini missions received effective doses up to ~3 mSv. Astronauts on the Apollo and STS missions had effective doses as high as ~5 mSv, whereas doses during space station missions were up to ~50 mSv according to estimates based on TLD doses.

The complicated mixture of radiation types in space makes organ dose estimates based solely on physical measurements somewhat uncertain, especially because of the nuclear absorption and production processes that occur as nuclei pass through tissue (Cucinotta, 2001; Cucinotta *et al.*, 2006). As a consequence, TLD measurements of radiation exposure may not be representative of organ dose equivalents (NCRP, 2002). In contrast, use of chromosome aberrations in peripheral blood lymphocytes as a biological dosimeter accounts for tissue shielding and orientation effects relative to variation in spacecraft shielding. The TLD doses were compared to those obtained using this biological dosimeter which was calibrated for each individual astronaut by irradiating preflight lymphocytes with gamma rays. In general, relatively good agreement was obtained between the effective doses that were calculated based on thermoluminescent dosimeter measurements and the biological dosimeter. It should be noted that caution should be exercised with regard to the use of lymphocytes as a biological dosimeter for use in risk assessments. Chromosome aberrations may be good predictors of dose, but not necessarily of risk (Brooks, 1999; 2001; Brooks *et al.*, 2003), although some recent studies are debating this (*e.g.*, Bonassi *et al.*, 2000; 2008).

Other improvements in the accuracy of dose estimates for astronauts also may come from new computational modeling approaches that define organ boundaries and the outer body contour using combinations of nonuniform rational basis spline and polygon mesh surfaces. This approach uses segmented CT and micro-CT images of human skeletal tissues to construct highly detailed virtual anatomical models. Radiation fields can be simulated within these models using track structure computer programs such as EGS4 thereby enabling detailed dose estimates for a variety of anatomical structures within the body. Use of such models within the context of the space radiation environment may be helpful in dose reconstruction and mission planning (Pafundi *et al.*, 2009).

2.2.4 Radiation Exposures During Jet Aircraft Flights

Air travelers are exposed to cosmic radiation levels that are higher than the cosmic plus terrestrial radiation levels normally encountered on the ground. In the contiguous United States at ground level, the average dose equivalent rate from cosmic plus terrestrial radiation is $0.06 \mu\text{Sv h}^{-1}$ (NCRP, 1987b). At an altitude of 10.7 km, for example, the dose equivalent rate from cosmic rays is $\sim 6 \mu\text{Sv h}^{-1}$ (O'Brien *et al.*, 1999). To maintain flight status, astronaut pilots must fly jet aircraft at least 15 h month⁻¹ and mission specialist astronauts must fly 4 h month⁻¹. Therefore, airline pilots may receive $\sim 3 \text{ mSv y}^{-1}$ (NCRP, 2009) and mission specialist astronauts may receive $\sim 0.3 \text{ mSv y}^{-1}$ during jet aircraft training flights.

2.3 Key Issues

The following bulleted list provides a brief comparison of radiation exposures that are discussed in this section:

- ubiquitous background radiation exposures received by human populations:
 - 3.1 mSv y^{-1} U.S. average annual ubiquitous background exposure; and
 - 30 mSv y^{-1} ubiquitous background exposures in Kerala, India.
- medical radiation exposures received by U.S. population:
 - 3.1 mSv y^{-1} U.S. average medical exposure;
 - 1 to 30 mSv per scan for CT scans;
 - 0.01 to 70 mSv per scan for nuclear medicine scans; and
 - up to 4,000 mGy skin doses from interventional radiology procedures.
- occupational radiation exposures received by U.S. workers:
 - 2 mSv y^{-1} U.S. average nuclear power worker;
 - 3 mSv y^{-1} airline pilots; and
 - 1 mSv y^{-1} average for medical occupational exposures.
- astronauts' radiation exposures:
 - 10 mSv for a 10 d space shuttle mission; and
 - 110 mSv for a 180 d space station mission.

3. Biology Pertinent to Variations in Individual Susceptibility with Respect to Radiation Risks for Astronauts

3.1 Overview

The purpose of this section is to:

- explore biological factors contributing to variation in radiation-sensitivity that may be of particular concern for NASA;
- address the impact of variation in genetic susceptibility of individual astronauts to both early and late effects following space radiation exposures;
- explore the possibility of identifying individuals of significantly higher or lower radiation sensitivity relative to the average using currently available methods and technology; and
- provide a scientific basis for evaluating pertinent legal and ethical issues regarding the flight status of individual astronauts. This information will be focused on astronauts in space, a relatively small group of men and women, in an age group ranging from ~30 to 50 y of age, who are highly selected for excellent physical and mental health and for skills that contribute to the likelihood of successful missions.

It is well known that genetic differences among individuals, even single-gene defects, as well as gender and age differences, can underlie relatively large variations in radiation sensitivity. For the purpose of this discussion, radiation sensitivity refers to the rate of change (increase) in the level of response for those effects, deterministic or stochastic, that depend upon the genetic makeup of the individual. The extreme cases are rare and the phenotypes are generally so severe that they are clinically obvious. These individuals would not likely be among the astronaut population. The homozygous recessive disease known as ataxia-telangiectasia (A-T) is the best known example of such a condition (Taylor *et al.*, 1975). While

the number of individuals in the population who are heterozygous for such defective genes can be orders of magnitude higher (Lavin and Shiloh, 1997) and may show mild radiation hyper-sensitivity (Chen *et al.*, 1978; Kato *et al.*, 2006a; 2006b; Nagasawa *et al.*, 1987; Scott *et al.*, 1993), these heterozygotes are not clinically obvious. Nevertheless, new technologies are emerging that can identify A-T heterozygotes (*e.g.*, Concannon *et al.*, 2008) but the overall impact of heterozygosity at the ataxia-telangiectasia mutated (ATM) gene locus on radiation sensitivity remains unclear. It should be reiterated that affected A-T individuals (homozygous recessives) would never physically qualify to be astronauts.

Despite the rapid advances in genomics and genome sequencing capabilities, and the fact that a growing list of genes known to affect radiation sensitivity phenotypes for many different biological effects of radiation, including molecular, chromosomal, signal transduction associated growth-regulating changes, cell killing, animal tissue and tumor acute and late effects, and animal carcinogenesis, there is still no knowledge that would allow a direct connection to be drawn between sequence changes that may be observed and a corresponding change in radiosensitivity. While such observed changes do not prove the alteration of any of these genes also may affect carcinogenic radiosensitivity for humans, it does suggest that it may be the case, and that it would be unreasonable to rule this out. Eventually it may be possible to identify significant numbers of genes and the particular mutations for defective alleles that have an overriding influence on the susceptibility of individuals to radiation-induced cancer, but such knowledge is not currently available. It also is likely that combinations of more subtle genetic changes in different genetic backgrounds can lead to an even wider range of radiation sensitivities among individuals. But progress in our ability to identify the position of a particular individual in a broad sensitivity spectrum is even more difficult to predict. Thus, it is not possible at present nor is it likely in the near foreseeable future to identify astronauts who have increased radiation risks due to genetic susceptibility (ICRP, 1999).

3.2 Average Risks for Radiation-Induced Diseases of Concern for Astronauts

The health effects of principal concern for occupationally exposed individuals such as astronauts working in space missions would include: carcinogenesis, cataracts, temporary sterility, and noncancer mortality. In addition, heritable effects would be of concern not only to the individual astronaut, but also to the other parent and affected offspring. At the present time, radiation risks are

determined from population studies and represent the average for that population. The epidemiological data available do not permit estimates of the dispersion of relative risk around the mean for the population so it is not possible for individuals to know whether their risk might be higher or lower than average. This Report reviews the scientific basis for, and the impact of, genetic susceptibility on individual radiation risk.

3.2.1 *Cancer Risk*

Numerous previous reports and summaries (ICRP, 1991a; NA/NRC, 1990; 2006; NCRP, 1993a; 1993b; UNSCEAR, 1994; 2000; 2008; 2009) have addressed the kinds of human health risks associated with radiation and have concluded that cancer induction is the major concern following low and moderate radiation exposures such as those found in LEO and deeper space missions conducted to date. The foundation for all quantitative cancer risk assessment is based on human epidemiology studies. Results from these studies, however, only predict average expectations of risk for similar populations and do not provide specific information pertinent to sensitive or resistant individuals or subpopulations. NASA has used this risk information to set a limit for the lifetime increase in the astronaut's fatal cancer risk due to occupational exposures at 3 %. This limit is in accord with risk estimates for protracted radiation exposures of 4 % Sv⁻¹ (NCRP, 1993a; 1993b) used in most occupational radiation protection programs. It has been noted that NASA no longer uses excess lifetime risk to set dose limits but rather uses risk of exposure-induced death (REID) (Section 6.2.3). It should be pointed out that the excess lifetime risk of cancer incidence and excess lifetime risk of cancer mortality are two different measures. Specifically, an individual may get a cancer (incidence) that can be reasonably attributed to a radiation exposure even if some form of medical treatment later prevents a death from occurring from that particular cancer.

From an epidemiological standpoint, any increase in cancer frequency in the current or former NASA astronaut population due to radiation exposure in space is not likely measurable. The size of the population is, and likely always will be, small and even without added radiation exposure there is already a high and variable risk among individuals comprising human populations (Pharoah *et al.*, 2002; Ponder, 2001). Aside from SPEs during missions, the predicted levels of radiation exposure associated with space travel, based on the predominantly LEO missions to date, correspond to a very low predicted increase in the frequency of radiation-induced cancer. For a significant SPE during a deep-space mission, such as

a space flight to Mars, the probability of causation can be modeled and then calculated.

3.2.2 Heritable Risk

That ionizing radiation produces mutations is well known, and the sensitivity for this effect has been studied extensively in various biological systems ranging from prokaryotic microorganisms to eukaryotes such as yeast, *Drosophila*, plants, and mammals (e.g., Searle, 1974; Thacker and Cox, 1984). There are major differences in the mutational dose and dose-rate responses between these organisms, but the induced frequencies per unit dose are sufficiently low that they would be difficult to be easily resolved in human epidemiological studies. It is also possible or even likely that differences in mutational sensitivity are different among mammals, and particularly between mice and humans (Bouffler *et al.*, 2006). This question has been examined for humans in epidemiological studies and, in fact, no heritable changes due to radiation exposure have been demonstrated in any human population.

The increased risk of cancer in the offspring of humans irradiated preconception appears to be very low if it exists at all. No excess cancer incidence has been reported in children born to parents exposed to the atomic bombings in Japan (Izumi *et al.*, 2003a; 2003b) or in the offspring of cancer patients treated with radiation therapy (Byrne *et al.*, 1998; Hawkins *et al.*, 1995). In their seventh report, the U.K. Committee on Medical Aspects of Radiation in the Environment (COMARE, 2002) reviewed the evidence concerning the incidence of childhood leukemia and other cancers in the offspring of parents occupationally exposed to radiation prior to conception (Neel and Schull, 1991). COMARE agreed that while it was possible in principle, thus far, the epidemiological evidence from the offspring of radiation workers in the United Kingdom, United States, and Germany has failed to establish a significant dose-related increase in the incidence of solid tumors, leukemia or non-Hodgkin's lymphoma in children.

In their eighth report, COMARE (2004) further concluded that the available epidemiological data were inadequate to allow definitive statements to be made regarding adverse pregnancy outcomes following preconception exposure of parental gametes to ionizing radiation in humans. This was due to difficulties in obtaining reliable figures for the biological effects of concern and to the possibility that the radiation exposures in most studies may have been too low to produce a statistically detectable effect. The conclusion reached by COMARE was that from all the epidemiological data examined, there was little statistically significant evidence to

establish that adverse reproductive outcomes in general are related to parental radiation exposures. Similarly, the limited data available did not link miscarriage or neonatal death with parental irradiation. The small population sample size and low dose levels involved in almost all of the published human studies on pregnancy outcome following parental exposure to radiation lack statistical power. COMARE did point out, however, that based on expectations from animal data this does not mean there are no effects. At the same time, the study did serve to show the risk for such effects in humans is not likely to be appreciably higher than that seen for animal studies.

However, there have been a number of reports of heritable effects occurring in the progeny of irradiated parents as measured by analysis of alterations in tandem repetitive deoxyribonucleic acid (DNA) sequences, such as minisatellite DNA and expanded simple tandem repeat sequences in the genome. Minisatellites are tandem repeat loci, typically 0.5 to 30 kb long, with repeat units in the range of 6 to 100 base pairs, whereas expanded simple tandem repeat sequences are composed of long arrays, up to 16 kb in length, of short (<10 base pairs) repeat units. Both types of loci have high spontaneous rates of mutation, which facilitate the measurement of induced mutation in relatively small numbers of samples. Recently a group of scientific experts reviewed all of the data on radiation associated germ-line mutation as measured by alterations in repetitive DNA sequences obtained by molecular analysis of tandemly repeated DNA loci in humans and expanded simple tandem repeat sequences in mice (Bouffler *et al.*, 2006). They acknowledged that radiation-induced transgenerational changes have been observed in mice, but concluded that while some studies (particularly those including exposure to internally-deposited radioactive materials) indicate that tandemly repeated DNA loci mutation could be used as a marker of human exposure, most human studies were negative. They also acknowledged that some minisatellite variants associated with human disease may affect gene transcription but causal relationships have not yet been established. Their overall recommendation was that the mutation data from human tandemly repeated DNA loci do not warrant a dramatic revision of germ line or cancer risk estimates for radiation over those currently in existence (Bouffler *et al.*, 2006).

3.2.3 Embryo and Fetal Risk

The major hazard for radiation-induced developmental defects occurs for exposures received during early development of the embryo and fetus. When the embryo is between two to five weeks

of age, during organogenesis, an increase in the risk for congenital malformations has been observed even for doses as low as 0.2 Gy (Brent, 2007). For later times, between 8 to 15 weeks of gestation, the risk for development of microencephaly and mental retardation is increased. This risk remains elevated albeit at one fourth that rate from 15 to 25 weeks. After 25 weeks, the risk returns to very close to the background level and is not detectably elevated in populations exposed during this stage of development. Although the ethics and legality of testing for pregnancy prior to space flight and preventing pregnant women from space travel are questionable, such a practice would minimize this risk.

3.2.4 *Other Risks Associated with Radiation Exposure*

In addition to cancer, there are several other types of risk associated with exposure to radiations that are of concern to astronauts. These are usually associated with high doses of radiation, well in excess of what an astronaut is likely to be exposed to. They include radiation sickness and death associated with the so-called prodromal radiation syndrome, as well as cataracts, temporary sterility, and noncancer mortality. However, it is possible that a very large SPE could result in whole-body radiation doses that could produce acute radiation sickness and acute health effects from the prodromal radiation syndrome. Some of the early effects, such as the prodromal radiation syndrome, are primarily related to relatively high radiation doses that result in extensive cell killing, tissue disorganization and depletion of essential cell populations. The acute whole-body absorbed dose required to kill 50 % of the human population is 3 to 4 Gy without medical intervention, which is very much higher than the doses ($\sim 1 \text{ mSv d}^{-1}$) that have been observed or predicted for flights in LEO during periods when significant SPEs have not occurred. It should be noted that although mGy-Eq should be used instead of millisievert for deterministic effects, a reader cannot know all the factors that were used in deriving millisievert due to lack of knowledge regarding the w_{R} radiation quality factors, distribution of different radiation types, and the dose and dose rate effectiveness factor (DDREF) used to convert absorbed dose in gray to effective dose in sievert for this space environment (LEO). Details of the doses predicted and measured are reviewed in Section 2. With the exception of these types of very large SPEs, the acute lethal effects from radiation exposure in space are of limited concern, with or without differences in genetic susceptibility.

NASA has expressed a great concern for radiation-induced cataracts in the lens of the eye since there is some indication that extended space flights with exposure to HZE may have resulted in