CHAPTER 11

RISK OF SKIN CANCER FROM SPACE RADIATION

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ABSTRACT

We review the methods for estimating the probability of increased incidence of skin cancers from space radiation exposure, and describe some of the individual factors that may contribute to risk projection models, including skin pigment, and synergistic effects of combined ionizing and UV exposure. The steep dose gradients from trapped electrons, protons, and heavy ions radiation during EVA and limitations in EVA dosimetry are important factors for projecting skin cancer risk of astronauts. We estimate that the probability of increased skin cancer risk varies more than 10-fold for individual astronauts and that the risk of skin cancer could exceed 1% for future lunar base operations for astronauts with light skin color and hair. Limitations in physical dosimetry in estimating the distribution of dose at the skin suggest that new biodosimetry methods be developed for responding to accidental overexposure of the skin during future space missions.

INTRODUCTION

In this report, we summarize issues important for estimating skin cancer risks on space missions. NASA's career dose limits set an upper level of acceptable fatal cancer to an increased risk of 3%. Risk assessment models are used to describe gender- and age-dependent dose to risk conversion factors. Short-term limits for protection of the skin, lens, and BFOs (NCRP, 2000) are levied to prevent the occurrence of acute health effects such as skin ulceration, moist and dry desquamation, and erythema. The threshold doses for skin damage and corresponding dose limits (1.5 Gy-Eq in 30 days and 3.0 Gy-Eq in 1-year) are such that it is difficult to find a mission scenario for LEO where these limits would be exceeded. For exploration missions to the moon or Mars, such possibilities exist if effective shielding and operational warning systems are not in place. The scientific basis for the deterministic dose limits are well established, originating in fairly extensive human data for skin reactions following exposures to both low- and high-LET radiation (NCRP, 2000). There is also a risk of late effects from ionizing radiation exposure of the skin, namely carcinogenesis. Because cancer risks projections for protons and heavy ions are highly uncertain (Cucinotta *et al.,* 2001) and individual factors play a prominent role in the incidence of skin cancers, the inclusion of such factors in risk assessment approaches is warranted.

BIOLOGICAL FACTORS IN SKIN CARCINOGENESIS

There are three major types of skin cancers: melanoma, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC). The incidence of skin cancer has risen dramatically in the 20^{th} century due to increased UV exposures from changes in clothing and other lifestyle factors. Melanoma is the most serious of the skin cancers; about 37,000 new cases of melanoma are reported annually in the U.S. (Kamb and Herlyn, 1998). Early detection is effective for assuring high cure rates with 5-year survival rates above 85% for these cases. However, if untreated, advanced stages of melanoma can metastasize and lead to fatalities with common secondary sites of brain, bone, lung, and liver. BCC and SCC are the more prevalent skin cancers and, in fact, are the most common of all cancers in the U.S. with about 750,000 cases of BCC and about 150,000 of SCC reported annually (Rees, 1998). However,

BCC is largely noninvasive with less than 1 in 4,000 cases undergoing metastasis. Metastasis rates for SCC are about 1 in 100 cases; however, fatalities are much smaller than for melanoma. Under-reporting or lack of histological confirmation of skin cancers, especially BCC and SCC, is a common problem and leads to uncertainties in estimates of UV or ionizing radiation risks. Tumor registers typically only track melanoma because of these problems.

Melanomas originate from the pigment-producing (melanin) melanocyte cells in the skin. The number density of melanocytes does not vary with skin color; rather the amount of melanin pigment is reduced in dark skin (Kamb and Herlyn, 1998). Melanocytes develop from progenitor cells in the central nervous system, reside at the interface between the epidermal and dermal layers of the skin, and form aggressive tumors when fully transformed. Genetic damage to melanocytes are causative of melanomas with disruption of the restriction point early in the cell cycle through mutations in cell cycle inhibitors such as the p16 protein, cyclin-dependent kinases, and the pRb protein, a key factor in their formation. Loss of heterozygosity and point mutations, efficiently produced by UV radiation, are common steps in tumor formation.

The more prevalent BCC and SCC originate in the keratinocyte cells of the skin. Point mutations in tumor suppressor genes, efficiently produced by UV exposure, are a common factor in BCC. However, aneuploidy is rare and BCCs are typically diploid. In contrast, the more aggressive SCC shows aneuploidy in a majority of the cases (Rees, 1998). For both BCC and SCC, point mutations in the p53 gene are a common event, with loss of heterozygosity of the p53 locus occurring frequently for SCC. Differences in the types of DNA damage produced by UV and ionizing radiation will be consequential in the probabilities for the induction of these specific skin cancer types. Genetic disorders account for less than 1% of skin cancers, however skin color plays a major role, with over a 10-fold difference increase in incidence for those with fair complexion and red or blonde hair compared to those with dark skin and dark hair.

RADIATION EPIDEMIOLOGY OF SKIN CANCERS

Two-epidemiology studies that can be used to form the basis of skin cancer risk estimates are the lifespan study of about Japanese 85,000 survivors of the atomic bombs (Preston *et al.*, 1994), and the study of 2,226 persons treated in childhood with 100 kVp X-rays to the scalp for treatment of tinea capitis (Shore *et al.,* 1984). In these studies, evidence for an association between ionizing radiation and BCC is quite strong, modest for SCC, and nonexistent for melanoma. For estimating skin cancer risks to astronauts, the differences in susceptibility of the Japanese, the role of UV exposures, and the different molecular lesions produced by high-LET radiation in space are important factors that lead to uncertainties in skin cancer risk from space radiation.

In the tinea capitis study, doses at the scalp ranged from 3.3 to 6.0 Gy, however significant doses were received in other areas, including 0.1 to 0.5 Gy to the face and neck, where many excess cancers were observed. No skin cancers were observed in the subset of black patients in this study. For white patients, a linear dose response is observed with an apparent synergistic effect from combined UV and X-ray exposure with 3.3×10^{-5} cases per cm^2 per PY-Gy in areas exposed to UV and X-rays, and 0.71×10^{-5} cases per cm^2 per PY-Gy in areas exposed to X-rays alone. This indicates about a fivefold enhancement due to synergistic effects with UV exposure.

In the Japanese study, fits to dose response data using a linear, linear-quadratic, or spline fit could not be distinguished (Thompson *et al.*, 1994). For the linear-fit an excess relative risk (ERR) of 1.0 per Sv with 95% confidence intervals of [0.41, 1.89] are found (Thompson *et al.*, 1994), which is one of the highest for all solid tumors found in this study. The ERR is found to decrease with age at exposure, but little dependence on attained age and gender were found. The average latency time for low-LET X-rays and gamma rays is on the order of 20 years.

Further, breakdown of skin cancer risk based on skin pigment is not possible based on existing epidemiology data. However, it is reasonable to assume that the UV interaction observed with X-rays would be influenced by skin pigmentation, such that skin cancer risk is dependent on skin color as well as area of the skin irradiated. Recently, studies of increased skin cancer risk have been reported amongst pilots (Hammar *et al.,* 2002). It is unclear if this increase is due to a synergistic effect between UV and atmospheric radiation, or if other factors such as the effects of altered circadian rhythms on melatonin regulation are involved. Another factor unique to spaceflight is the differences in UV exposure in space. Outside the Earth's atmosphere, all three UV components are present (UVA, UVB, and UVC). The risk of skin cancer from this spectrum, atypical to that on Earth, combined with the space radiation environment has not been studied.

Burns *et al.* (1994) studied radiation-induced skin tumors with high-LET radiation, using a rat model. In these studies, electrons are used as a low-LET radiation. A linear-quadratic model or threshold model best fits the data for electrons and a linear response is found for heavy ions. For electrons, a dose-rate reduction is observed following split dose experiments, however, a dose enhancement is observed for tumors induced by high-LET argon ions. Because the low-dose response for electrons is difficult to quantify, estimates of relative biological effectiveness factors for heavy ions are highly uncertain, with values as low as 10 or higher than 100 possible, which are dependent on the method used to extrapolate the electron response data to low doses and dose-rates. The use of radiation quality factors to estimate skin cancer risks is intermediate between such reductions of the rat skin tumor data for heavy ions.

ESTIMATES OF SKIN CANCER RISK FOR SPACE MISSIONS

For transferring of cancer risks across populations, one can use multiplicative risk, additive risk, or mixture models. The NCRP risk model for solid cancer used by NASA (NCRP, 2002) uses a mixture model based on averaging the multiplicative and additive risk models in transferring risk coefficients from the Japanese to the U.S. population. Thompson *et al.* (1994) has noted that the multiplicative model may be preferred for skin cancers, such that an additive or mixture model would underestimate the risk for whites with fair skin and hair in the U.S. Skin cancer rates vary substantially based on race, ethnicity, and UV exposure. Age-adjusted-rates for the incidence of melanoma in whites living in Hawaii and Connecticut are 45.6×10^5 and 21.6×10^5, respectively, and for blacks living in these same states 0.42×10^5 and 1.31×10^5, respectively. In the additive risk model, the ERR expressed as an induction rate per Sv, α, and the baseline rate in the Japanese population, B_{Japan}, is used to directly estimate the ERR in the US population as,

$$ERR_{additive} = \alpha B_{Japan} \quad (1)$$

In the multiplicative model, the ERR is estimated using the induction coefficient for the Japanese population times the baseline rate in the U.S., B_{US}

$$ERR_{multiplicative} = \alpha B_{US} \quad (2)$$

and the NCRP preferred model is to average the results of Equation (1) and (2) (NCRP, 2000). In the limit of $B_{US}/B_{Japan} >> 1$, it can be shown that the mixture model underestimates the multiplicative model by twofold. Since the multiplicative model is preferred for skin cancer excess incidence (Thompson *et al.* (1994)), we assume a twofold increase for the average U.S. white population over the incidence rates provided by the NCRP (NCRP, 2000). Based on other studies noted by Thompson *et al.* (1994), we estimate at least a further twofold increase for U.S. whites of fair skin and hair color. Also, we assume a fivefold increase in risk for skin areas with high UV exposure and that such areas cover about 10% of the skin area. In **Table 11-1**, we show risk estimates for the excess incidence of non-melanoma skin cancer per cm^2 per Gy using the multiplicative model and the more conservative estimates for males with fair skin and hair at regions receiving combined UV and space radiation. For this estimate, we assume the surface area of the skin of 2 m^2 appropriate for the 50% percentile height and weight male.

The range of doses to be experienced on space missions varies substantially with the mission parameters. For nominal EVAs in LEO, skin doses of 0.1 mSv can be expected. Doses of 1 to 10 mSv are possible following frequent geomagnetic storms due to enhancement of the electron belts. Doses during the largest SPEs in LEO could reach as high as 100 mSv inside the spacecraft and could exceed dose limits on EVAs. Mission doses on ISS can exceed 200 mSv near solar minimum. For an 8-hour EVA on the surface of the Moon, doses exceeding 1,000 mSv are possible (Kim *et al.,* 1999). Note that, although the occurrence of more than a few large SPEs (>4) per solar cycle is highly unlikely, small to medium SPEs occur with a frequency of several per month at the peak of the solar cycle (Shea and Smart, 1990). The cumulative effect of such frequent SPEs could substantially increase skin doses to astronauts working at future lunar bases. Using the estimates of **Table 11-1**, one would expect that astronauts with high susceptibility would have skin cancer risks exceeding 1%. The results of **Table 11-1** can be used with transport codes and computerized anatomical geometry models to estimate the distribution of skin cancer risks for specific space missions.

Table 11-1. Estimates of Percent Excess Non-Melanoma Skin Cancer Risk for Low-Dose Rate Exposure of 1,000 mSv Delivered in Less Than 1 Year for Whites of Differential Skin Pigmentation With or Without UV Exposure*

	Whole body averages for excess risk per Sv		Partial skin averages for excess risk per Sv per cm^2	
Age, y	Average U.S. White	U.S. White, fair skin & hair	U.S. White, fair skin & hair (no UV exposure)	U.S. White, fair skin & hair (synergistic UV exposure)
25	0.96	1.92	0.69×10^{-4}	3.46×10^{-4}
35	0.72	1.54	0.54	2.77
45	0.16	0.32	0.11	0.58
55	0.1	0.2	0.07	0.36

*Assumes total skin surface area of 20,000 cm^2

A persistent problem for EVA is the limitations in EVA dosimetry, including its ability to detect steep dose gradients at the less shielded skin areas, such as the arms, hands, and face. Skin doses for soft proton or electron

spectra could vary more than fivefold at various locations of the skin. Since these least-shielded areas also receive the highest UV exposures, they will have an appreciable probability for skin cancer risk. Biodosimetry (George *et al.*, 2001) provides an alternative approach to estimate radiation exposure in accidental situations. Biodosimetry using cytogenetic methods could be used to validate a high exposure, however methods for performing these assays on skin plugs would need to be developed and the development of protocols to observe base damage or other biomarkers of skin cancer precursor would also be useful. For individuals of light skin color, biodosimetry methods should be pursued in order to improve the understanding of risk estimates, and to ensure adequate preparation for emergency responses to adverse radiation situations.

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