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Malignancies Associated with Radiation in Aerospace Personnel-A Review of Evidence and Studies

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Abstract

It is no secret in the realm of Aerospace Medicine that radiation is considered to be a hazard to the health and safety of personnel such as astronauts, pilots, aircrew members, flight attendants and so on and so forth. The forms of radiation to which such individuals are constantly exposed to include extra-vehicular radiation e.g. UV and cosmic radiation and radiation emitted from onboard apparatuses, fuel etc.

Now, it is thought that the former (i.e. extra-vehicular radiation) poses more health risks to humans upon exposure in comparison to the latter. These risks include the development of malignancies, teratogenicity, mutagenicity and non-cancerous tissue damage e.g. cataracts. It is essential to appreciate the fact that the inhabitants of earth who do not engage in frequent air/space travel are protected to a certain extent from the above mentioned deleterious effects. Such protection is primarily received by means of the earth's magnetic field and the atmosphere. Individuals who fly at high altitudes e.g. commercial pilots and aircrew members are less protected, especially if flight routes are high latitude (i.e. further away from the equator). Their counterparts in space (astronauts) however are not subject to this protection at all during occupation, and thus are potentially exposed to greater magnitudes of extra-vehicular ionising radiation.

Keywords: Malignancies; Radiation; Melanoma; Leukemia; Breast cancer

Introduction

We are all aware that an assortment of cancers can occur after prolonged and frequent exposure to ionizing radiation. Nevertheless, the most commonly documented cases occurring within aerospace personnel include malignant skin melanomas, leukemias and breast carcinomas.

Before we can begin to discuss the influence of radiation on these three types of malignancies it is important that we acquire

a brief understanding of the nature of extra-vehicular ionizing radiation, its detection, and current recommendations regarding occupational exposure. Being electromagnetic in origin, it is no surprise that this radiation consists of a range of wavelengths varying from low frequency microwave radiation to infrared, UV and up to high frequency X-ray and γ -radiation and beyond. It is probably easier to qualify the forms of ionizing radiation that have the highest potential in causing harm to aerospace personnel as being either cosmic, UV or magnetically trapped.

Cosmic radiation as a whole is further subdivided into galactic cosmic radiation (GCR) and energy particles from solar particle events (SPEs). Galactic Cosmic Radiation is predominantly "particulate", consisting of α and β particles as well as heavier nuclei such as tin and lithium. On the other hand, Solar Particle Event Radiation consists of high energy protons formed as a result of magnetic disturbances on the sun's surface. Estimation of the former is much more practicable in comparison to the latter [1]. Owing to the fact that the geomagnetosphere does not cover the Earth's Polar Regions, aircraft/spacecraft travelling in these regions are exposed to greater amounts of GCR.

As the National Aeronautics and Space Administration (NASA) makes plans for manned missions to Mars, the problem of radiation protection becomes a major issue. According to Cucinotta and Durante [2], "every cell in an astronaut's body would be hit by a proton or 2° electrons every few days and high ionizing energy particles (HZE ions) approximately once per month". This would provide a significant potential for carcinogenesis in astronauts involved in such exploration.

Extra-vehicular radiation especially that of cosmic origin can be quantified in terms of dose equivalent. This is basically the amount of radiation that causes a biological effect on an exposed individual and is measured in Sieverts (Sv). As we may be aware, ionizing radiation may be monitored via 3 methods [3]. These include after-flight dosimeters, personal dosimeters and calculations done by SIEVERT flight plans.

The Federal Aviation Administration (FAA) has recommended that aircrew members be exposed to no more than 20 mSv per year for a 5 years average, with no more than 50 mSv in a single year [4]. Workers (including non-aerospace personnel) who are

considered to be receiving more than 6 mSv per year should be individually followed-up and assessed as well as have exposure rates kept on record. Such recommendations have been made by the National Radiological Protection Board (NRPB) of the UK.

Knowing such background information, it is inevitable that a number of questions will surface in our minds pertaining to possible malignancy occurrences in the abovementioned population. Hence the aim of this review is to attempt to determine whether an association exists between radiation (particularly extra-vehicular) exposure and the 3 types of malignancies outlined previously.

Such findings could contribute towards raising awareness and appreciation of these medical problems. As the time for commercial human space flight and space tourism quickly approaches, the possibility of carcinogenesis could eventually become a risk factor [1,5,6]. This could have an assortment of impacts such as medical certification of space tourists and disclosure of cancer risks prior to embarkation.

Types of Studies

In this review, a number of articles were examined. The predominant types were cohort and case-controlled studies. A number of laboratory and animal studies were taken into consideration.

In order to compliment the above, a few other forms of literature such as meta-analyses, expert reviews and commentaries were examined.

With regards to the cohort and case-controlled studies, only ones whereby participants were aerospace personnel were included (i.e. participants that were astronauts, pilots, flight attendants or any other occupation within air/space vehicles). In general, studies portraying outcomes pertaining to malignant skin melanoma, leukemia and breast cancer were focused on in detail.

It should be noted that only studies, in which participants being exposed to a minimum of 20 mSv/yr for a minimum of 5 years were in considered. Of these, only those published from 1990 to present were dealt with. Studies were acquired via the US National Library of Medicine search system.

Discussion

Before examining the research and evidence that deals directly with malignant skin melanoma, leukemias and breast cancer; we should briefly take into account, a few general studies that illustrate laboratory findings and mortality rates from cancer in the mentioned personnel.

Firstly, there have been laboratory studies conducted whereby human cells radiated with high ionizing energy particles (HZE ions) showed neoplastic transformation. Basically HZE ions are contained in radiation fields in space. Bennet used HZE ions in the form of heavy charged particles (obtained from NASA's Space Radiation Laboratory) to model cosmic radiation [7]. The cells used in this experiment were cultured fibroblasts. Likewise, experiments involving shielding of such cells from HZE ions were

also conducted [8]. These experiments showed a decrease in cell transformation with increasing thickness of shielding with a number of different materials. Such attenuation has supported the association between cosmic radiation (and thus extra-vehicular radiation) and tumor genesis. It should be noted that materials such as aluminum and lead have known to be incorporated into space suits of astronauts as alluded to by Cucinotta et al. [9] who conducted shielding effectiveness evaluations for reducing space cancer risks.

With regards to cancer mortality, a collaborative cohort involving 8 countries was published [10]. Focusing on cancer deaths in male airline cabin attendants in Europe, it was found that the overall cancer mortality and the mortality from malignant skin melanoma were significantly increased. In contrast, there was an overall decrease in cancer mortality in their female counterparts. The mortality from breast cancer in female cabin attendants was increased but not to a significant extent.

Interestingly, Zeeb and colleagues concluded that there was no increase in cancer mortality that could have been attributable to cosmic radiation. This however does not rule out the probability that other extra-vehicular radiation e.g. UV radiation, may have played a role in cancer mortality within the above study group.

Having appreciated the findings from cellular studies and overall cancer mortality analyses in aerospace personnel such as cabin attendants, we can examine research that has been done with regards to the three specific malignancies outlined earlier.

Malignant Melanoma (Skin)

The increased risk of this type of carcinoma has been evident predominantly in populations involved in frequent air travel such as pilots and aircrew.

A cohort involving 10,211 pilots from Nordic countries (Iceland, Sweden, Denmark, Norway and Finland) was conducted in 2003. In this study, it was found that there was increased incidence of malignant skin melanoma in pilots who flew more than 5000 block hours (hours per annum) [11]. Additionally, Pukkala and colleagues found that the relative risk of skin melanoma arising on the trunks of participants in the study, significantly increased with increasing exposure to estimated radiation. This was the case in individuals exposed to more than 20 mSv/year. Below is the research group's results, indicating number of cases observed, number of cases expected and significant standardized incidence ratios (SIRs) of each cancer site they examined (**Table 1**).

Results from another study involving cockpit crew (i.e. pilots and flight engineers) from 9 European countries showed that there was increased mortality from malignant melanoma [12]. These results were consistent at least up to the time of publication, with findings that malignant skin melanoma did occur in pilots, owing to the effects of radiation exposure.

A meta-analysis conducted by researchers from the Swiss Air Force Institute of Aviation Medicine indicated that 7 out of 8 studies examined showed an increase risk for aviators to

develop malignant melanoma [13]. Unfortunately, the authors alluded to the fact that there was lack of evidence (portrayed by the studies) that supported the hypothesis that cosmic radiation

was the cause of the melanoma seen within the study populations.

Table 1 It shows observed and expected numbers of skin melanoma cases and SIRs (standardized incidence ratios) with 95% confidence intervals (CI) among male pilots in the Nordic countries. Reproduced with permission. Courtesy of ©2003 Aerospace Medical Association.

Type of Skin Melanoma	Whole Cohort			
	Observed	Expected	SIR	95%CI
Head and neck	7	2.81	2.49	1.00-5.14
Trunk	32	13.7	2.33	1.60-3.30
Limbs	14	6.12	2.29	1.25-3.84
Skin melanoma (all sites)	56	24.4	2.29	1.73-2.98

Of course there have been a few negative findings in studies aimed at investigating a causal relationship between radiation and malignant melanoma in aerospace personnel. According to Boice et al. [14], an earlier 1995 study involving 1 700 Finnish Flight attendants, most of whom were female, showed that the incidence of melanoma was not significantly elevated. Likewise, another meta-analysis illustrated a decrease in the risk of malignant skin melanoma in male military and civilian pilots [15].

Leukemias

There are a few animal studies that have led us to believe so far that radiation of aerospace origin could play a causative role in leukemias. Comparisons between heavy-particle carbon ion and X-ray induced lymphomas in B6C3F1 mice were made, and it was found that there was a higher frequency of loss of heterozygosity (LOH) on chromosome 11 in mice exposed to the former type of radiation [16]. It is renowned from previous studies that chromosome 11 LOH is a feature of lymphomas in numerous strains of mice [17].

It is therefore no surprise that Nicholas et al. [18] identified chromosomal aberrations in peripheral lymphocytes in the blood samples of male, non-smoker pilots based in Toronto. Fluorescent *in situ* Hybridization (FISH) was done and the mean aberration frequency was 3 times higher in the pilot group in contrast to the non-airline control group.

With reference to astronauts, at least 2 studies have been done to assess chromosomal aberrations. Within 3 of 12 astronauts that took part, researchers found clonal aberrations in blood lymphocyte chromosomes [19]. Upon follow-up, such quantities of aberrations decreased. Such evidence suggests a strong temporal relationship between extra-vehicular radiation and chromosomal aberrations. As chromosomal aberrations/damage are precursors for hematological malignancy (i.e. lymphomas), it would be reasonable to infer that radiation exposure in aerospace personnel could predispose to lymphoma genesis. Unfortunately this is not supported by Horstmann et al. [20], who concluded that space radiation does not induce a significant increase of intra-chromosomal changes after

conducting FISH studies on 11 astronauts' blood lymphocytes. However the group failed to address any possibility of inter-chromosomal changes.

A number of authoritarians have acknowledged a relationship between extra-vehicular radiation of cosmic origin and acute myeloid leukemia (AML). It was actually reported that a 5 to 1 fold increase in incidence of AML was attributed to cosmic ray exposure [20]. Unfortunately, more recent studies have refuted this indicating that the incidence of AML in airline pilots is not significantly higher than that in the general population [21].

Nevertheless, results from case studies published by Gundestrup et al. [22] have shown deletion of the long arm of chromosome 7 in aircrew members is strongly associated with AML. Gundestrup and colleagues studied the cytogenetics of seven aircrew members who had AML, and compared this to the karyotypes of 19 published cases of AML and myelodysplasia which involved radiotherapy alone.

A previous population-based cohort study done by the same group, showed that male cockpit crew members in jets flying more than 5000 hours have significantly increased frequencies of AML [23].

Breast Cancer

Owing to the trend that breast cancer is predominantly more common in females than males; the vast majority of studies investigating the effects of ionizing radiation involve female cabin attendants and pilots.

Meta-analyses have indeed shown increased incidence of breast cancer in the former. An example was that conducted by Buja et al. [24]. Bayesian hierarchical models were applied to the results of 7 published studies after standardized incidence ratios (SIRs) were estimated. Likewise similar results were portrayed by Tokomaru et al. [25]. From this said study, it was concluded additionally that UV radiation was an unlikely occupational risk for breast carcinoma.

Major research investigating the effects of extra-vehicular radiation on breast cancer in female astronauts has been if not extremely scarce, non-existent. This is due to the fact that such a

small population of women has flown in space. According to Barr et al. [26], it is insufficient to draw a statistically significant conclusion pertaining to the risk of breast cancer in such a female population.

Conclusion

As the evidence above is examined, it is not unreasonable to initially think that extra-vehicular radiation is a huge contributory factor for malignancies. Unfortunately to date, we still cannot find a direct association between the mentioned radiation and the 3 cancerous conditions discussed for a number of reasons. An assortment of confounding factors, limitations and problems are evident, the major ones of which are outlined below.

Firstly, none of the studies were able to directly ascertain the presence of extra-vehicular radiation in the doses received by personnel. There was no particular device that could have differentiated cosmic/UV from other sources of radiation. Hence the radiation to which participants were exposed could have been sourced to for example air/space craft fuel and communication equipment.

There are other limitations which cannot easily be prevented in relation to the studies investigating the exposure effects in all 3 cancers. Examples of these include age, ethnicity (genetic factors and predispositions), gender and so on and so forth. Such factors have the potential to facilitate carcinogenesis independent of radiation exposure.

Publication bias could have also played a role in the availability of current research available on malignancies in air and space personnel.

More specifically, with reference to malignant melanoma, individuals could have experienced increased sun exposure- many pilots are renowned for engaging in leisure activities e.g. being on a sunny beach etc. [13]. In these cases, UV radiation may be contributory- but this is at a terrestrial level; as opposed to being exposed to UV at altitude.

It is essential to appreciate the fact that breast cancer etiology apart from genetics, depends on numerous other factors e.g. nulliparity, smoking etc. [27-29]. These factors may not have been accounted for in the studies. As mentioned earlier the number of studies investigating breast cancer in female astronauts is scarce owing to the fact that very few women have travelled in space. More studies are warranted in this field and as the number of female astronauts increase, this would be achieved.

Additionally, chromosomal aberrations despite being an indicator for potential are not definitive of malignancy. Many leukemias develop without any chromosomal aberrations in hematological cells.

Finally, at this point it is impossible to confirm an association between extra-vehicular radiation and malignancies in aerospace personnel with regard to malignant skin melanoma, leukemias and breast cancer. In an effort to ascertain whether extra-vehicular radiation is implicated in the causation of

malignancies, vast scope for further research exists. More studies in both aircrew and astronaut populations are warranted, especially the latter. Even more emphasis should also be placed on conducting breast cancer research involving more female astronauts. Likewise, studies should involve a wider range of populations i.e. not just North American and Scandinavian personnel as predominantly seen in many of the above studies. Lastly it would be beneficial to attempt to develop a device that can estimate extra-vehicular radiation e.g. cosmic radiation directly from cabins.

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