



WHICH IS THE MOST RELIABLE MARKER TO ASSESS THE EFFECTS OF COSMIC RADIATION EXPOSURE IN POLISH MILITARY PILOTS: A MINI REVIEW OF LITERATURE

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Introduction: Military pilots, similar to civilian pilots and crew members, receive larger doses of ionizing radiation than the general population. Exposition to small doses of ionizing radiation at prolonged durations has been related to slightly higher incidence of certain cancers. However, fighter jet pilots from time to time flight their airplanes at even higher altitudes, thus exposing themselves to higher doses of more energetic radiation than their civilian counterparts. In this mini review we discuss the procedures involved in controlling the radiation exposure to military and civilian pilots, as well as air crews. Markers of radiation exposure are discussed. Based on available literature, it appears that the biological markers of radiation, i.e., markers related to the actual changes in tissues, account also for individual differences in anatomy and physiology, as well as individual differences in sensitivity and lifestyle, as jet engine emissions, electromagnetic fields from cockpit instruments, ultraviolet radiation, caradian rhythm disruption, etc.

This mini review concludes that biological dosimetry methods, i.e., counting frequencies of chromosomal aberrations, appears to be most suitable to evaluate exposure to ionizing radiation in military pilots.

Keywords: ionizing radiation, military aviation, dicentric chromosome assay

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INTRODUCTION

People are exposed to natural and human-made sources of radiation. Natural radiation originates from many sources. Additionally, people are exposed to cosmic radiation, particularly at high altitude. This extra radiation originates from high-energy particles of cosmic origin that collide with atmospheric particles, thus creating secondary radiation. Only a small fraction of energy of the primary particles reaches the surface of the Earth in form of secondary particles [29]. Therefore, airplane pilots and cabin crews at flight altitude are exposed to larger doses of ionizing radiation than the general population. Its dose varies in different parts of the world and based largely on the geomagnetic field, altitude, and solar cycle [17,29]. According to the United Nations UNSCEAR 2000 Report [37], airline flight crew workers receive more dose on average than any other worker, including workers of nuclear power plants (see below). The amount of radiation received by airline crews is higher if they routinely work flight routes close to the North or South Pole, where this type of radiation is maximal on our planet [17]. As the fighter jet pilots occasionally flight even at higher altitudes, they expose themselves to even higher rates of radiation [22]. They are also exposed to electro-magnetic fields (radars), not to mention other factors like stress or irregular work schedule.

This increased exposure to radiation by pilots and cabin crews causes quantitative biological effects [1,13,16,19,38]. Several articles have related work as a pilot and flight attendant with occupational cancer risk. A meta-analysis study of more than 250 thousand pilots and cabin crew determined a slightly increased standardized incidence ratio of melanoma and standardized mortality ratio for these flight based occupations, as compared to general population [34]. Another study found higher age-standardized incidence ratio of developing leukemia in a large cohort of Korean air transportation industry workers as compared to government employees and the entire population [24]. A study evaluating incidence and mortality of selected types of cancer among almost 35 thousand fighter aviators in the United States Air Force, who served between 1970 and 2004, found a slightly increased risk of developing and dying from melanoma skin cancer, prostate cancer, and non-Hodgkin lymphoma, as compared to the general population [43]. However, in a younger cohort of almost 5,000 fighter pilots who served between 1995 and 2017 (compared to age and sex matched officers) no increases in rates of malignant cancers

were observed [33]. This discrepancy is likely due to the fact that incidence rates for cancer increase (almost) exponentially with increasing age. In other words, the prevalence of cancer is higher in older cohorts. Consistent with this notion, the risk for cancers was shown to increase with an increase in number of employment years, cumulative air hours, and total cumulative radiation dose [15].

On the other hand, it should be remembered that except for cosmic radiation, aircraft workers are also exposed to various chemical and physical hazards, such as jet engine emissions, electromagnetic fields from cockpit instruments, ultraviolet radiation, circadian rhythm disruption, decreased atmospheric pressure and other volatile substances emanating from aircraft construction materials [24,41]. Another form of radiation that comes from the sun is ultraviolet (UV) radiation. However, UV radiation is not considered cosmic radiation. It is lower in energy and is considered non-ionizing radiation [28].

BACKGROUND AND IN-FLIGHT RADIATION

The general approach regarding radiation exposure in airline flight crew workers and military pilots is to obtain as low radiation exposure as it is technically and economically viable. The Federal Aviation Administration in their circular about inflight radiation exposure lays down the concept and nicknames it as "As Low As Reasonably Achievable" (ALARA) [11,40]. It is the basic principle in radiation protection. It assumes making every reasonable effort to maintain exposures to ionizing radiation as far below the dose limits as it is practical.

The effects of radiation can be estimated as the energy deposited in air, tissue, etc. by all types of ionizing radiation; they are measured in units called gray (Gy). This energy is called absorbed dose. The radiation damage from an absorbed dose depends on the type of radiation and the sensitivity of different tissues and organs. To account for these factors, effective dose was introduced. The unit of effective dose is sievert (Sv). The rate at which this dose is delivered (dose rate) is measured in units such as microsieverts per hour ($\mu\text{Sv}/\text{hour}$) or millisievert per year (mSv/year) [28].

At the sea level, the average radioactive exposure from all sources is approximately 3 mSv/year. Natural background radiation exposure contributes to about 2.4mSv/year, but these background

radiation levels vary geographically. Medical imaging and therapeutics is the largest man made source of exposure and contributes to about 0.6 mSv/year [32].

During air travel, the air crews and passengers are exposed to increased radiation from space as compared to sea level [4]. The 1991 International Committee of Radiation Protection recommendations require that cosmic radiation exposure for flight crew members should be assessed and recorded. Initially, ionizing radiation monitoring equipment was permanent in all Concorde due to its maximum operating altitude of nearly 18,000 m (59,000 feet), as cosmic radiation exposure increases with increasing flight altitude [22]. Another problem, which should be taken into account, is the systematic increase in the length of exposure during flights. The introduction of aircraft such as the Boeing 747-400, Airbus A330, and A340 has led to the development of ultra-long-haul flights lasting up to 18 hours or more.

On a single route, the lowest measured dose rate was 3 μ Sv per hour during a Paris-Buenos Aires flight and the highest rates were 6.6 μ Sv per hour during a Paris to Tokyo flight and 9.7 μ Sv per hour on the Concorde in 1996–1997 [8]. However, the dosages may vary, e.g., during periods of high solar activity [4]. The United States Federal Aviation Administration (FAA) requires airlines to provide flight crew with information about cosmic radiation. Based on collected data, radiation levels experienced by flight crews are well below current occupational limits recommended by the International Commission on Radiological Protection and the Federal Aviation Administration of 20 mSv per year (averaged over five years) [30,42], with a maximum in one year of 50 mSv [4]. In fact, the average annual effective dose for cabin crews in the nineteen nineties was 2.27 mSv and, for long-distance flight captains, it was 2.19 mSv [30]. Newer data suggest that the dose can be even smaller. The mean annual effective dose in German pilots was estimated to be on average 2.25 mSv (range 0.01–6.39 mSv) [45]. Similar values were obtained for American air crew members [14] and Czech pilots [23]. Even during maximum galactic radiation conditions in 2009, no Canadian pilot received more than 6 mSv in one year [5]. Per comparison, the recommendation for the general public is no more than 1 mSv per year [17]. In 1991, the International Commission on Radiological Protection recommended that exposures to natural cosmic radiation should be considered occupational exposures for aircrews (ICRP 1991) [17].

EFFECTS OF IONIZING RADIATION ON BIOLOGICAL TISSUES

Ionizing radiation can impair the functioning of tissues and/or organs. It can produce acute effects such as skin redness, hair loss, radiation burns. However, significant increase of cancer risk was reported at effective doses above 100 mSv [1], which are not encountered in aviation. However, the radiation dose accumulates in the bodies of pilots and air crews over the years. It should be noted that if the radiation dose is low and/or it is delivered over a long period of time (low dose rate), the risk of developing cancer is significantly lower thanks to repairing mechanisms. Nonetheless there is still a risk of long-term effects, but they may appear years or even decades after the exposure [27]. The repair mechanisms were researched in animal models, mostly rodents or gene-modified rodents, as well as cell cultures. However, the findings cannot be directly translated to humans, as e.g., rodents are more resistant to biological effects of radiation as compared to humans [27]. In general, the studies suggest that environmental radiation is needed to develop and maintain the defense response to the effects of radiation in cells.

DEVICES TO MEASURE DOSES OF IONIZING RADIATION

There is no single device that can satisfactorily measure the entire range of energies and types of particles. Multiple devices have been used to measure ionizing radiation dose in aircraft and they were named in a publication by the European Radiation Dosimetry Group in 1996 [9]. There are three main types of methods for measuring ionizing radiation doses: passive dosimetry, active dosimetry and biological dosimetry.

Passive dosimetry involves recording the dose of radiation received by the dosimeter. A common feature of passive dosimeters is the recording of only the cumulative dose over a period of time and the subsequent reading under laboratory conditions. They are mostly simple and inexpensive, widespread in the study of personnel exposed to small doses of radiation in working conditions, such as radiology personnel in hospitals, who are normally exposed to very small doses of radiation, and greater exposure occurs only in emergency situations. A variation of personal passive dosimeters are electrostatic dosimeters; the displacement of the threads is proportional to

the absorbed ionizing radiation dose. This type is represented, for example, by the DKP-50 military dosimeter. A significant disadvantage is the low sensitivity of this device.

Active dosimetry can be based on gamma-sensitive gaseous counters (Geiger-Müller), scintillation counters, or proportional tissue equivalent counters. The devices can be set up to indicate both actual radiation dose and dose equivalent. Active dosimetry primarily allows measurement of instantaneous radiation intensity, but it is possible to determine cumulative dose using memory systems. The disadvantages of this type of dosimeters are usually significantly larger dimensions than passive dosimeters and significantly higher price.

In the past, to calculate the exposure, physical phantoms composed of materials with properties resembling human tissue were used. However, they use was expensive and offered only a crude approximation of human body. Currently, computational phantoms, i.e., mathematical models of human anatomy are available [2]. They provide more realistic approximation of human anatomy, e.g., they facilitate inclusion of anthropometric parameters such as body weight, height, as well as inclusion of involuntary motion, such as respiration or cardiac cycle. Even creation of individualized phantoms in radiation therapy is now possible. However, the physical markers of radiation exposure cannot account for individual susceptibility to the effects of ionizing radiation. Recent reports suggest that the Tissue Equivalent Proportional Counter (TEPC) may be the most suitable device to measure the absorbed dose in aviation, although it is not calibrated over the entire energy spectrum [9].

BIOLOGICAL DOSIMETRY

Biological dosimetry, also named biodosimetry, is based on evaluation of changes to biological tissues that are related to the radiation dose [31]. Ionizing radiation is able to cause large-scale structural rearrangements to the genome. It also has effects on molecular and cellular levels, gene expression, cell cycle and regulation of epigenetic mechanisms [27]. There are several biomarkers used in genotoxicity studies and for monitoring purposes. They are based on damage to both deoxyribonucleic acid (DNA), chromosome and proteins. DNA damage induced by ionizing radiation includes double and single-strand breaks, base damage (BD) and DNA/protein crosslinks [16]. It should be noted that the ionizing parti-

cle usually causes loss/damage of a sequence of nucleotides in the incident. Ionizing radiation uniquely produces DNA double-strand breaks (DSBs) randomly throughout the genome. There are certain mechanisms allowing for recovery of the damaged material (e.g., [35]), but, sometimes, the process is not successful. It results in “misrepairs” that may lead to morphological changes in chromosomes that are called chromosomal aberrations (CAs). They are thought to be the result of misrejoining of DSBs. CAs are considered one of the most sensitive and reliable biomarkers of exposure to ionizing radiation [21].

The structural aberrations are divided into unstable and stable ones. The latter type of aberrations is passed down to daughter cells in mitosis and tend to accumulate with repeated or chronic exposure, while the unstable are not [19]. Therefore, the number of stable structural aberration (e.g., translocations and insertions) does not decrease with time, and they are more suitable to evaluate chronic exposure to genotoxic agents, such as ionizing radiation. Conversely, the frequency of unstable aberrations (such as dicentric chromosomes and acentric fragments) will slightly decrease in time after a one-time exposure.

Interestingly, increased frequency of CAs was detected in hospital workers at risk of chronic exposure to low doses of ionizing radiation (<100mSv) [19] or just after a single abdomen computed tomography (CT) scan [1,13,38]. The changes are detected in lymphocytes. Interestingly, there are reports that such damage in animal models might be also induced by electromagnetic fields [18], which are present on board of airplanes.

The damage of nuclei by ionizing radiation may lead to split of the nucleus and creation of extra-nuclear bodies (micronuclei), which contain fragments of chromosomes [36]. Discussion of micronuclei is outside of the scope of this review, as a large dose of more than 0.5 Gy (far more than encountered in aviation) are needed to create a detectable level of micronuclei.

Dicentric chromosome assay (DCA) is a well-established biodosimetry test used to estimate exposure to ionizing radiation. Dicentric chromosomes are considered to be specific to radiation [25]. They are not affected by electromagnetic fields [18]. Measurement of radiation-specific dicentric chromosomes in peripheral blood lymphocytes is currently the gold-standard for radiation biodosimetry [26]. To our knowledge, only this method has been utilized to assess radiation-induced DNA changes in civil flight personnel. One study demonstrated changes [6], while two

did not [10,44]. Both studies used small samples: 21 and 40 participants, respectively. However, use of antioxidants appeared to have a protective role against creation of dicentric chromosomes [10].

In humans, dicentric chromosomes occur naturally in substantial portion of the population [39]. Nonetheless, as the background levels of dicentric chromosomes are low in non-exposed individuals, the DCA is able to assess irradiation doses as low as 0.1 Gy ([25] and references therein). The test of the frequency of dicentric chromosomes in peripheral blood lymphocytes allows even to assess the absorbed dose of radiation in an individual.

DCA is a very specific measure of radiation induced effects. Increase in dicentric chromosome formation was shown after a single abdomen computed tomography (CT) scan both in teenagers [13,38] and adults [1]. The dose was estimated to be around 50 mSv.

Biological tests take into account not only occupational and/or environmental exposure but also inter-individual differences in sensitivity and lifestyle [7], as well as the other factors pilots and cabin crews are exposed to [19,24]. Similarly, the effects of flying at altitudes more than 10,000 m will be accounted for. Currently, little or inconclusive information on genotoxic effects due to chronic exposure at low dose in pilots and aircrew is available.

On the opposite, it should be noted that some animal studies reported susceptibility of the results to presence of psychological stress [20,41]. However, they utilized large rates of radiation over short time, which does not well reflect the situation of pilots and air-crews. Nonetheless, negative effects of stress on the ability to resist the effects of radiation in pilots and aircrews, especially in fighter pilots cannot be excluded.

DISCUSSION

This manuscript discusses the effects of ionizing radiation on airplane pilots, including military pilots, and cabin crews. These workers are exposed to increased doses of cosmic radiation at flight altitude, which likely lead to increased risk of certain cancers. To minimize the risk, the ALARA concept was introduced, which is the principle of keeping radiation exposure as low as reasonably achievable.

Both active and passive dosimetry allows only for measuring the absorbed dose. Biological dosimetry is able to measure the effects of ionizing

radiation on the body's cells as well. Various biomarkers, such as double and single-strand breaks, are used to measure exposure to ionizing radiation. However, the use of dicentric chromosome assay (DCA) is considered to be the gold standard for radiation dosimetry. DCA was used to evaluate radiation exposure in pilot in earlier studies.

On the contrary, there was a report of lowering the frequencies of translocations and of dicentric chromosomes in mice due to exposure to very low doses of ionizing radiation (gamma rays; 0.05 mGy/day) for between half a year and two years [21]. This is a dose comparable to the dose received by the pilots and aircrews on a long-haul intercontinental flight lasting about a dozen of hours or more. Similar phenomenon was reported in humans: the death rate from cancer in eight states in the USA with highest effective dose from natural sources is 2% to 26% lower than in the remaining 42 states [12]. Therefore, the exposure to higher radiation rates in aviation may turn out to be protective.

Furthermore, biological markers of radiation exposure account for psychological stress [20,41], as well as (some of them) for the effects of electromagnetic fields. Therefore, in future studies evaluating exposure to ionizing radiation in military pilots, it would be recommended to separate groups of military transportation/bomber pilots and fighter pilots, given the presence of radars on fighter jets. On the other hand, there is very little research on oncogenic properties of electromagnetic fields [3]. The radiation-induced injury accumulates over time, but the effect disappear over longer periods of time due to e.g. leucocytes turnover. Therefore, the marker is susceptible to auto-repairing processes.

Ionizing radiation in large exerts detrimental effects on human body. However, for small doses provided at low rates the situation is not clear, given the existence of repair mechanisms. It is worth mentioning that these mechanisms may be compromised by stress and other factors. Taken together, biological dosimetry methods counting frequencies of chromosomal aberrations appear to be most suitable to evaluate exposure to ionizing radiation in military pilots both from jet and transport aircraft branches of Polish Air Force. Although translocations are passed to daughter cells via mitosis and their number does not decrease with time, almost all of the previous studies in pilots and aircrews calculated frequencies of dicentric chromosomes.

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