RADIOBIOLOGY FOR SPACE RESEARCH

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1. Introduction

Life on earth has developed under gravity, humidity and atmospheric air pressure. In space, this environment has to be reproduced artificially in order to provide living conditions for the astronauts. The radiation environment, however, is present in both situations but differs in quality and intensity. On earth, the natural and artifical radiation is mainly caused by sparsely ionizing radiation like X- or γ-rays. Additionally, densely ionizing radiation is created by a few α-emitters like Radon. Altogether for both radiation qualities, the European average sums up to a mean dose of 1mSv per year. In space, the radiation burden is much bigger and depends on altitude and inclination of the space orbit. For high-altitude flights beyond the magnetic shielding of the earth, cosmic radiation i.e. high-energy particles from protons to iron ions predominate. Space radiation reaches its maximum values at a solar particle event where lethal doses can be delivered within an hour or less. These events, however, are rather unlikely. Much more important is the permanent ie. protracted exposure to the low-dose radiation of the heavy charged particles of cosmic glactic rays. Because of their high local dose these particles are able to create local damage in bio-molecules that can manifest itself in long-term alterations like genetic mutation and cancer induction. It is the induction of these biological changes that determines the general risk of long-term missions. For low-altitude flights such as MIR or space station orbits, trapped electrons and protons from solar origin predominate. To study the biological radiation response, especially genetic alterations and cancerogenesis, X-ray experiments can be performed in order to mimic sparsely ionizing electrons. And in order to gain more insight in the biological action of galactic cosmic rays, accelerator experiments are necessary.

2. The Radiation Field

Depending on the distance from earth the composition of the radiation field varies because particles are trapped in the geomagnetic field. At low earth orbit (LEO), trapped protons and electrons from the radiation belt predominate.

Apart from the cosmic galactic rays there are also the protons of solar eruption events, the solar flairs. These solar particle events are statiscally distributed and cannot be predicted to occur or not to occur during a specific space mission. But in the long run, a stable period of eleven years for maximum solar activity has been observed. During solar particle events, a dose of a fraction of one Gray up to the Gray region can be delivered in a short time of a few hours or even less. Therefore, solar particle events could be life threatening in extreme cases but viewed on a long-term basis, they are so rare that they contribute only with a small fraction to the general radiation burden.

The main contribution of dose during a space mission outside the magnetic shielding of the earth originates from the galactic cosmic rays (GCR) (fig. 1). GCR are heavy charged particles from the most frequent protons up to iron ions. Ions heavier than iron are several orders of magnitude less frequent since they originate from super nova explosions and cannot be synthesized by exo-thermic nuclear fusion reactions like iron and the elements being lighter than iron.

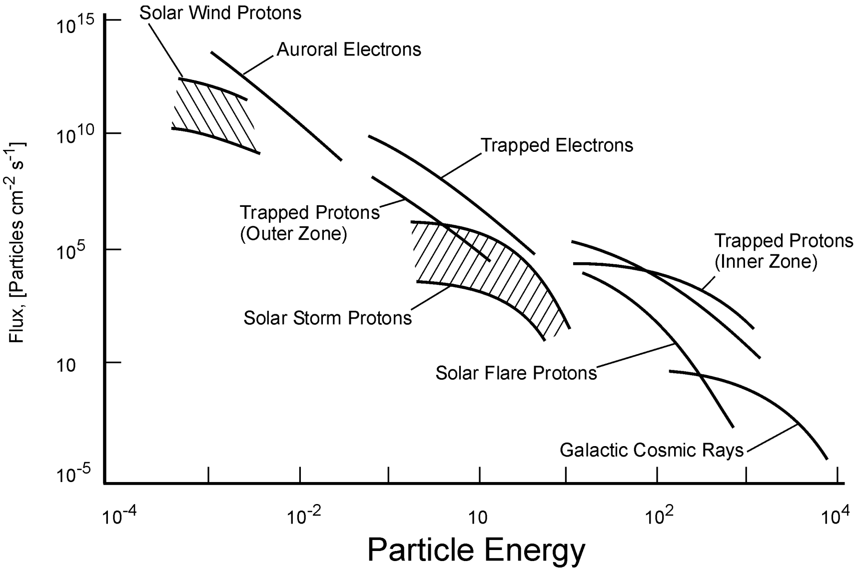

Figure 1: Spectrum of the different radiations as a function of energy in MeV (redrawn from Wilson 1991)

The galactic cosmic radiation has an energy spectrum with a broad maximum at a few hundred MeV per nucleon and a steep and continuous decay towards higher energies (fig. 2). This high-energy tail has been measured up to the TeV region and is a big problem for an effective shielding. Because the cross sections for nuclear fragmentation are still significant for the ions of these extremely high energies, any shielding layer introduced to stop the low-energy particles also produces showers of nuclear fragments from the high-energy particle impact.

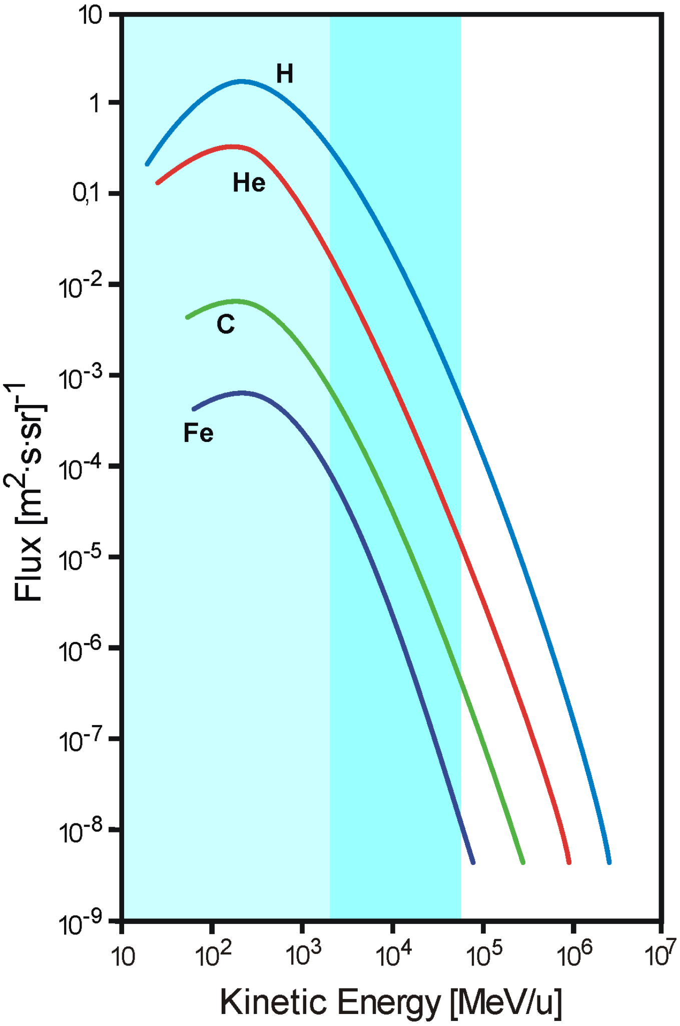

Figure 2: Kinetic energy of the galactic cosmic radiation (GCR) (adapted from Wilson 1991)

Transport calculations for the GCR spectrum in various shielding materials like aluminium showed that after a small benefit in the first thin shielding layers, thicker absorbers do not produce a net reduction of the biological effect that correlates reasonably with the increasing mass of the shielding material. The decrease in the amount of low-energy particles is almost compensated by the increase in nuclear fragmentation. For details of this very complex but important ion transport avalanches we ask the reader to refer to the comprehensive article by Wilson et al. 1991.

The fluence distribution of protons is three orders of magnitude higher than that of Fe-ions but the energy deposition, i.e. the dose of a single particle, depends on the square of the atomic number. Therefore, the difference between protons and iron in their frequency contribution is nearly compensated by the dose. Taking the change in the relative biological efficiency into account the fraction of iron particles becomes as important as that of protons. For low earth orbit (LEO), the total dose per day is about 1mSv behind a shielding of 1g/cm^2 of Aluminium. This is the average dose per year on earth. Spaceflights are on average 300 times more exposure-intensive than our daily life. But the actual value of a space mission very much depends on the altitude of the flight and on the inclination of the route. Because at the magnetic poles, shielding is drastically reduced and an orbit over the earth poles results in a greater exposure than an equatorial flight.

Outside the geomagnetic shielding the particle composition of the GCR becomes more relevant and the estimation of the biological effect is determined rather by the hit probability of the critical target inside the cells, i.e. the cell nuclei, than by a dose averaged over a long time. For example, a three years' mission to Mars was calculated to produce 400 proton and 40 He-ion traversals through the nucleus of each cell of the human body [2]. This number decreases for heavy ions like Fe to a hit probability of 3%. According to these statistics, every cell nucleus will be hit by a proton once every three days and by a He ion once every thirty days. Considering the high hit frequency and the large number of cells at risk it is very evident that a non-protracted exposure would be lethal while the distribution over a period of three years allows repair with a good chance of the traversed cells to survive. However, the long-term consequences like cancer induction or genetic mutation determine the risk. It is well-known that a macroscopic tumor may originate from only one transformed cell. If a single mutated cell survives cancer may develop. Consequently, cancer is determined more by the biological processing than by mere induction statistics of DNA damage.

3. Health effects resulting from cosmic radiation

Depending on dose, acute or long-term effects can be induced by radiation exposure. Acute effects like nausea, vomitting, skin irritation, depletion of white blood cells occur at doses of about 1.5 Gy or more. These high doses are produced by solar storms. Astronauts can be protected in storm shelters from the low-energy particles because these events are preceeded by an enhanced solar activity.

Long-term effects are genetic alterations, cancer induction, damage to the central nervous system and peripheral neurons and accelerated aging. Among these effects cancerogenesis and neural damage seems to be the most important. The uncertaincies for the risk determination with regard to long-term effcts are large and the risk estimation is mainly based on epidemiological data from the atomic bomb survivors (see A.M. Kellerer). However, the radiation quality in these historical data differs largely from that in the space radiation environment. Presently, our knowledge about the space radiation effects of low doses is compiled from different sources: There are the observations of astronauts returning from long-term space missions such as at MIR [3,4] or the previous moon expeditions. In addition, accelerator experiments are performed with human blood cells and various other cell types. In both cases, the induction of chromosome aberration is studied because it is believed to be the most accurate and sensitive indicator of genetic mutations in general and for cancer induction in particular.

Additional information is gained from the few accidental exposures of nuclear technology workers. But again, theses cases are rare and have another radiation quality than space radiation. A special problem is the continuous or protracted irradiation with low doses in space. This situation is completely different from an acute exposure in nuclear accidents and it is not possible, either, to simulate a many month protraction in cell experiments. Normally, the experiments are performed at high doses delivered in short time and model assumptions have to be made in order to extrapolate to low dose protracted exposure.

4. Biological Dosimetry

Chromosomes become visible when the cells divide and the DNA is distributed in equal proportions to the daughter cells. In this stage, DNA condenses to small bodies, the chromosomes, that are visible under the microscope. Pertinent DNA damage is expressed in chromosomal aberrations [3,4,5] .Chromosome damage is there-fore an indicator for DNA mutation and genetic alterat-ion. .

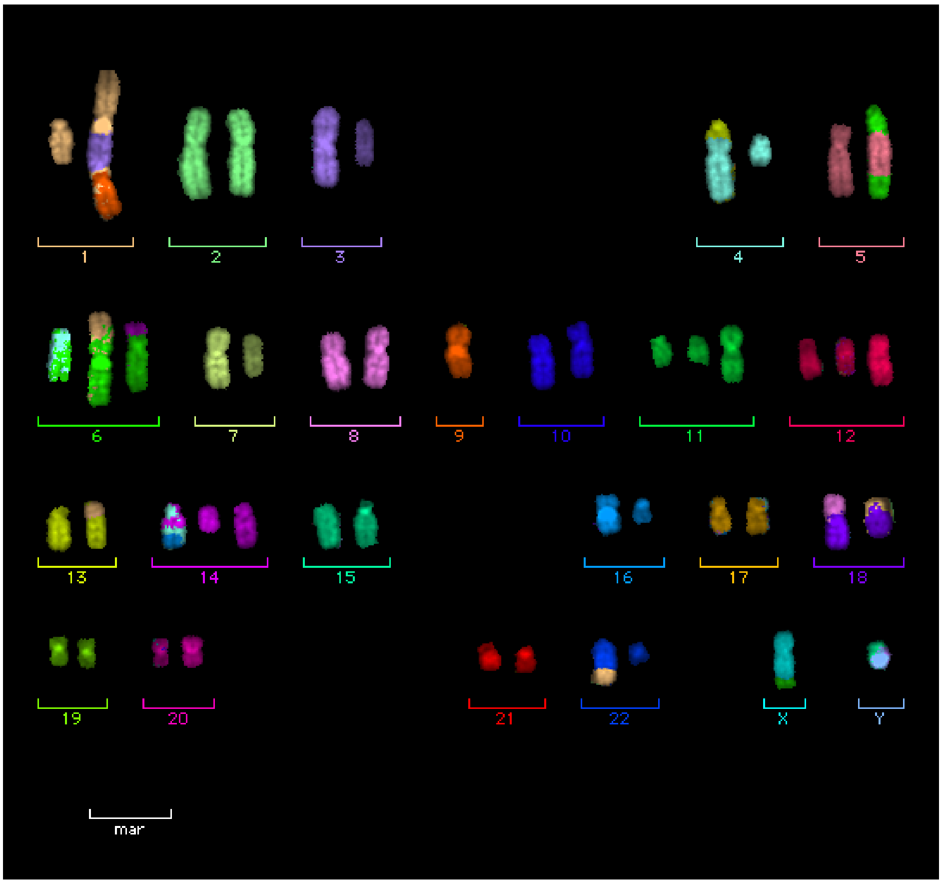

Figure 3: Originally, each chromosome pair is painted in one color. Chromosomes that are multicolored result from the interchange of parts of two or more different chromosomes. Cells showing translocations normally remain viable but may induce cancer if oncogenes are connected to strong promoters.

In the past, socalled non-transmissible

aberrations like rings or dicentrics have been used to measure chromo-somal changes because these aberrations are easy to score. However, cells carrying these aberrations have only a small chance to survive the next cell divisions and are not representative for DNA damage leading to long-term consequences. More recently, new techniques like chromosome painting [3,5] allow to study the induction of transmissible chromosome aberrations like translocations. Tranlsocations originate from at least two DNA double strand breaks that are misrepaired in one or two chromosomes (fig3). Since no genetic information is lost, cells carrying this new DNA configuration have a high chance to survive and pass the aberrations on to further cell generations. In addition, translocations are very frequently involved in the initiation of cancer, i.e. when a strong promotor is linked to an oncogen stimulating infinite cell growth.

The recent development of the Multicolor Fluorescence In Situ Hybridisation (M-FISH) allows to paint each chromosome in one sprecific color and to observe the exchange of material between chromosomes as shown in fig. 3.

5. Biodosimetry of exposed persons

Men returning from extended space missions, such as the moon expedition or extended stays at the MIR, carry chromosome aberrations in their blood cells as exemplarily shown in figure 4 and described in detail in the references [3,4]. However, it is almost impossible to deduce dose effect curves from these measurements. First, because the aberration rate is fortunately low and second, because the dose and particularly the composition of the radiation environment, i.e. the radiation quality, is not known in detail. It is possible, however, to analyze these data in model calculations using X-ray dose effect curves and quality weighting factors - and other plausible assumptions - in order to calculate expectated values for chromosome damage. Then, the prediction can be compared with the findings obtained from the blood analysis of the cosmonauts. Basic assumptions in these estimations have to be made for the extrapolation of partial or inhomogeneous exposure to total body exposure, from high dose rates to low dose rates and from X-rays to particles.

At least the last extrapolation, i.e. the change in radiation quality, can be studied in accelerator experiments where the differences in efficiency of particle radiation can be assessed. However, these experiments are very tedious. Due to the complexity of the particle-induced aberrations the time scale of their expression is drastically prolonged (see chapter on radiobiology) and it is difficult to obtain in vitro experimental data that can be used for risk estimation. Still, these accelerator experiments are the only source of reliable data that can help to understand the mechanics of genetic mutations and cancer induction. Therefore, the accelerators for nuclear and high-energy physics will always have a small but important experimental activity in radiobiology.

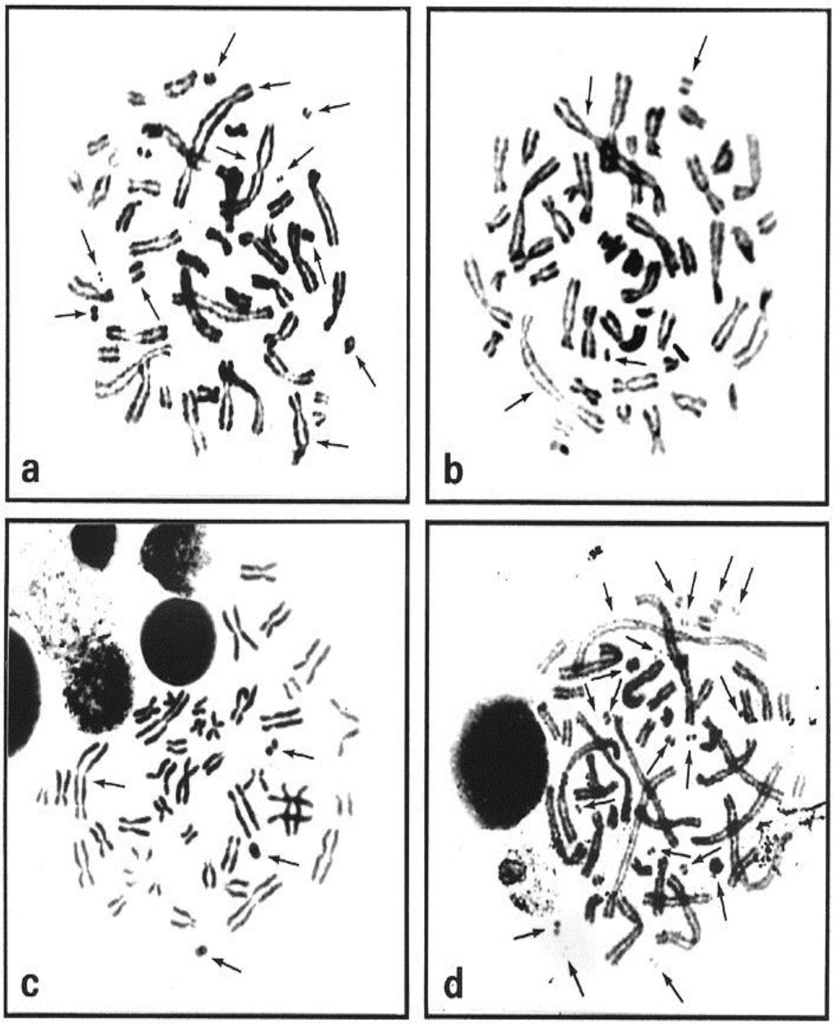

Figure 4: Lymphocyte chromosomes of a Russian cosmonaut clearly show aberrations after a 6-months MIR mission. Arrows indicate the chromosome aberrations detected in these cells.

6. Conclusions

Human beings in space are exposed in average to a radiation dose that is 300 times as high as on earth, thus receiving a daily exposure that equals the radiation burden of one year on earth. In addition, space radiation is different from the radiation environment down here in its quality and is dominated by high-energy particles. It is proven that this radiation exposure produce genetic alterations including cancer. Other stress factors of space travels like microgravity, gas environment, artificial nutrition also generate biological and physical impairments. But physiological recovery is reached shortly after landing. Regarding genetic damage transmissible chromosome aberrations are pertinently present during the stay and thereafter. Up to now, the mechanisms and the extent of this damage is not known in detail. To the day, only high-energy particle accelerators for nuclear physics experiments allow to study these questions in detail being the only source of information that allows to optimize the shielding conditions for man in space.

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