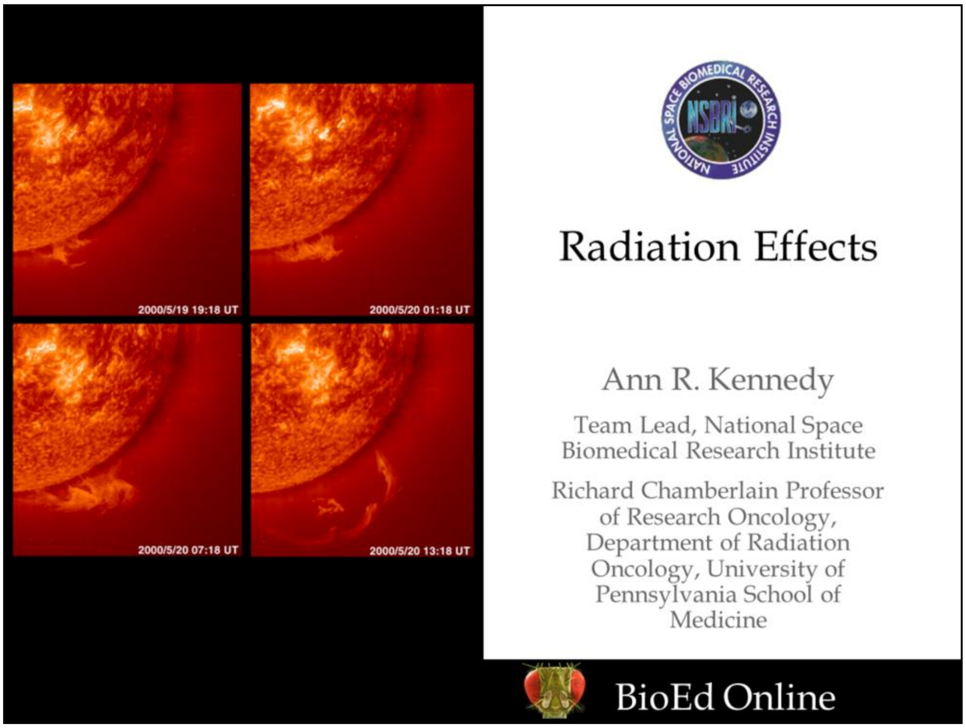


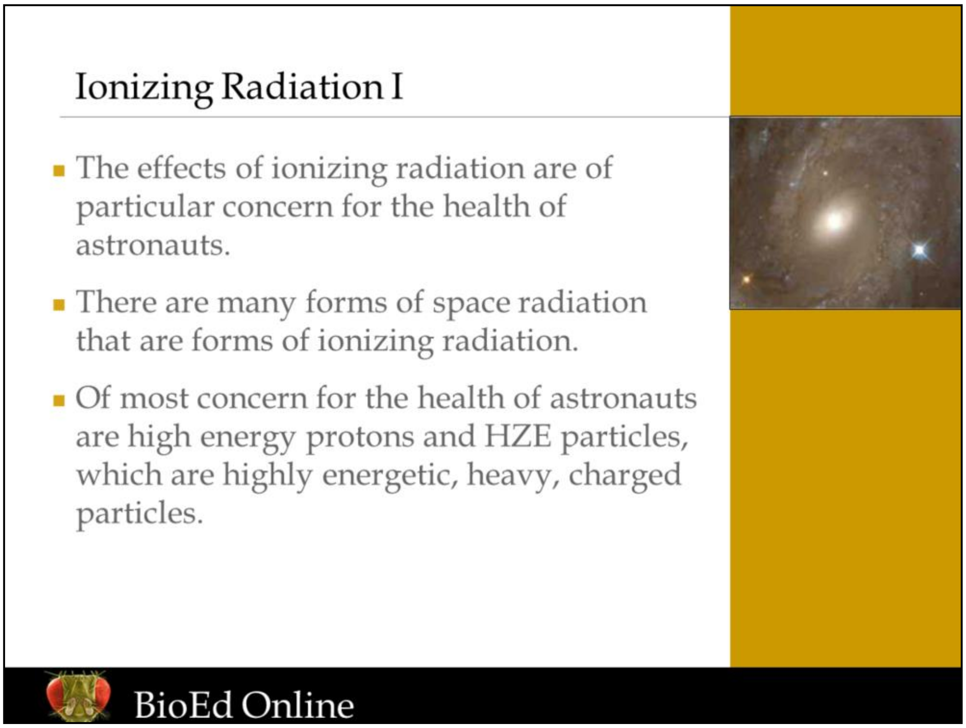
Transcript:

My name is Ann Kennedy, and I am a Professor of Radiation Biology at the University of Pennsylvania School of Medicine.

Image Reference:

NASA. (2000). *Four consecutive EIT images showing the evolution of a prominence in the bottom right quadrant of the sun*. Retrieved 06-15-2008 from http://www.nasa.gov/multimedia/imagegallery/

This work is supported through NASA Cooperative Agreement NCC9-58 with the National Space Biomedical Research Institute.

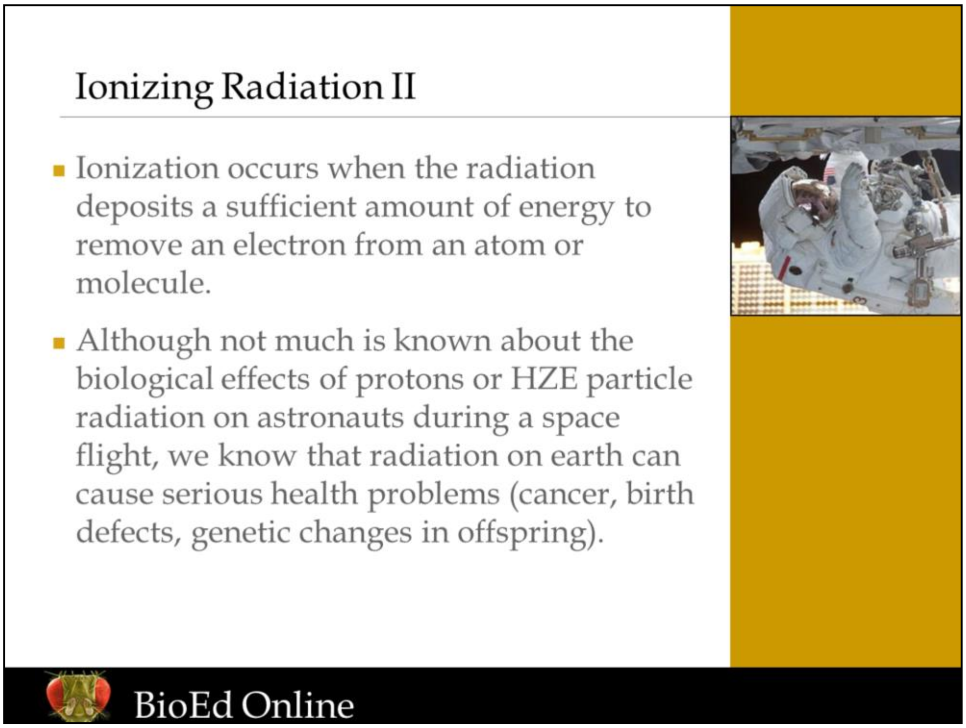


Transcript:

Today I am going to talk with you about the hazards associated with exposure to the types of radiation encountered by astronauts during space travel. While we are all exposed to low doses of radiation in our environment—which includes the air we breathe, the water we drink and the foods we eat—the radiation encountered during space travel will expose astronauts to higher doses of radiation, and more varied types of radiation, than those encountered on earth. Two types of radiation which are encountered by astronauts during space travel—protons and highly energetic, heavy charged particles known as HZE particles—are not encountered by people on earth and are of particular concern for the health of astronauts. Very little is known about the biological effects of these types of radiation. We do, however, know quite a lot about the biologic effects of other types of radiation.

Image References:

NASA. (2000). *Space radiation*. Retrieved 06-15-2008 from http://www.nasa.gov/multimedia/imagegallery/



Transcript:

The types of radiation of most concern for the production of biological effects are called ionizing radiations. Ionizing radiation has the ability to penetrate deeply into our bodies and damage critical biomolecules, in our tissues, that are needed to function properly. The deposition of energy from ionizing radiation results in the ejection of electrons from atoms within cells, which then results in the ionization of atoms in the cell. Such ionizations are only the first event in a chain of chemical reactions that lead to the known biologic effects of radiation, some of which you have probably heard of, like the induction of cancer and birth defects, and the production of alterations in the DNA of our germ cells (which can lead to heritable genetic changes in our offspring). It is expected that the major biological effects of radiation are brought about by changes in the DNA of our cells, the basic units of structure and function in biological systems. So measurements of DNA damage figure prominently in radiation biology research.

Image References:

NASA. *Space walk.* Retrieved 06-15-2008 from http://spaceflight.nasa.gov/shuttle/support/researching/radiation/brochure1/

NASA Space Radiation Laboratory

- The effects of heavy ion radiation in biological systems are studied at the NASA Space Radiation Laboratory (NSRL).

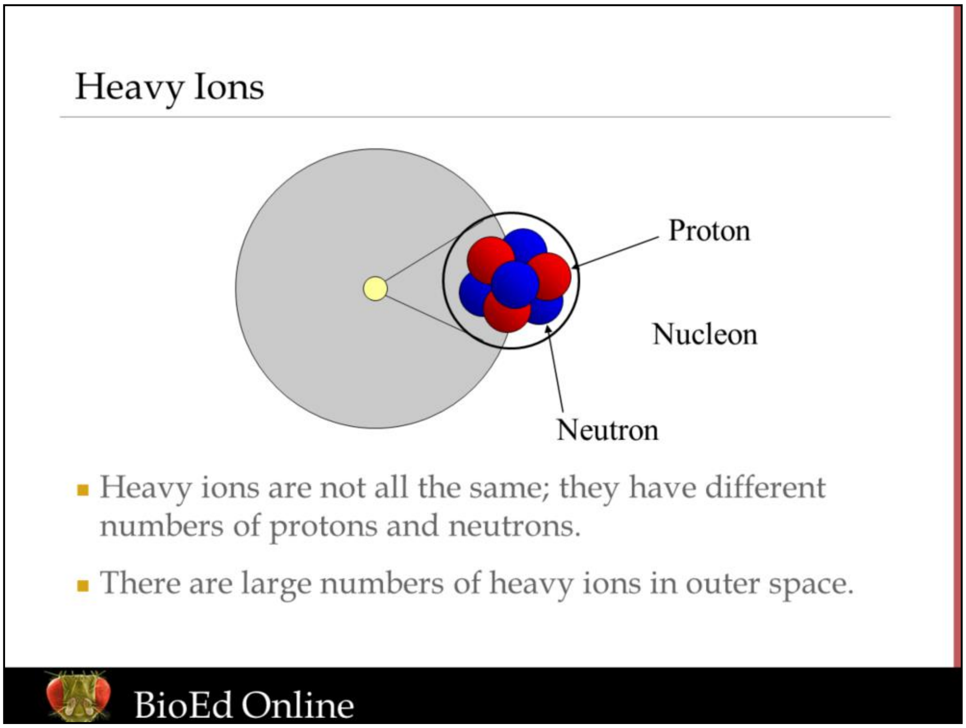
BioEd Online

Transcript:

Many different types of radiation encountered during space travel could produce adverse biological effects in astronauts. Exposure to ionizing radiation during space travel poses some unique hazards, however, primarily due to the presence of relatively large numbers of heavy ions in space. Although we are not exposed to heavy ions on earth, we can study their biological effects at the NASA Space Radiation Laboratory, known as NSRL, which is a facility at the Brookhaven National Laboratory in Upton, New York. NSRL provides beam lines of the energetic heavy ions encountered during space travel to support studies on the biologic effects of these types of radiations.

Image Reference:

NASA. National Space Radiation Laboratory. Retrieved 06-15-2008 from http://hacd.jsc.nasa.gov/web_docs/radiation/newsletters/V2-1.htm

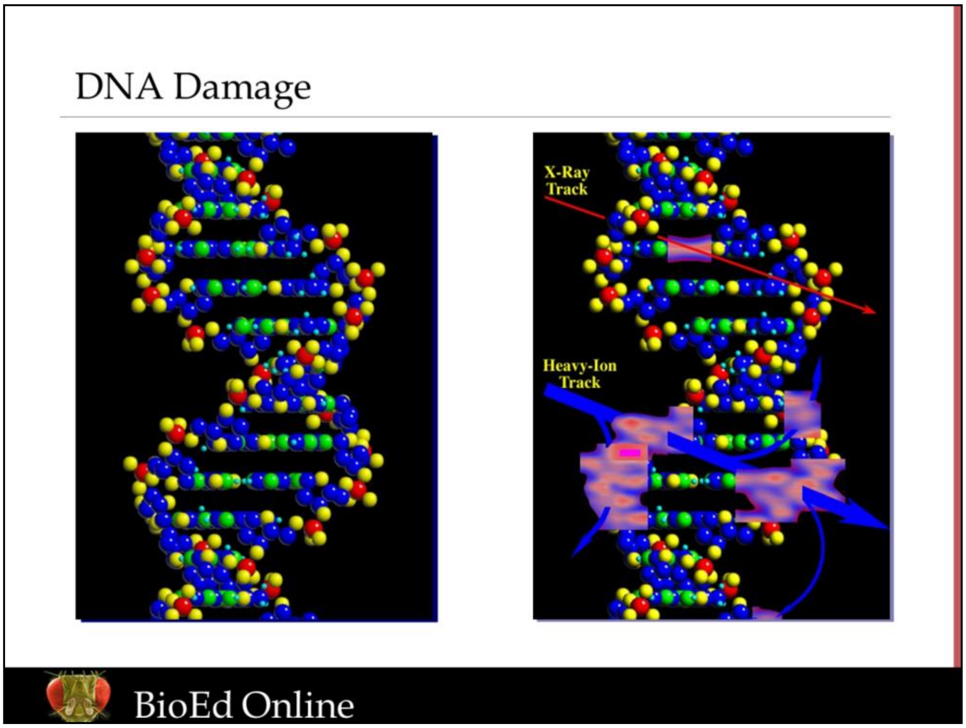


Transcript:

Heavy ions contain different numbers of protons and neutrons (called nucleons) in the nucleus of atoms, and large numbers of these heavy ions are found in outer space.

Image Reference:

Rusek, Adam. *Heavy Ions in Space*. By permission.



Transcript:

Iron ions, frequently used as the HZE particles, as well as other heavy ions, produce relatively large amounts of DNA damage, as their track width is considerably greater than that produced by x- and gamma radiations.

A major question in space radiation research concerns how the expected biological effects of space radiations can be minimized. Theoretically, it would seem possible to eliminate the effects of heavy ions through shielding methods. Shielding for heavy ion exposure, however, is extremely difficult as it is complicated by nuclear fragmentation, in which the secondary fragments produced from heavy ion interactions can be equally or more hazardous to biologic tissues than the original heavy ion.

Image Reference:

NASA. (2000). *DNA Damage*. Retrieved 06-15-2008 from http://www.nasa.gov/audience/foreducators/postsecondary/features/F_Space_Radiation_Project.html

Pertinent Radiation Terminology I

- Radiation doses are expressed in terms of the energy absorbed per unit weight, which is related to the number of ionizations produced within a tissue.
  - The unit of radiation dose is the gray (joules/kilogram)
- The linear energy transfer (LET) is a measure of ionization density.
  - Expressed in units of electron volts deposited in tissue per micrometer of track length
  - Low LET: x-rays, gamma rays, and beta particles
  - High LET: neutrons and alpha particles

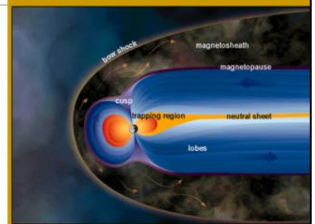
Transcript:

To account for the biological effectiveness of different kinds of radiation, it is necessary to define some of the related terms. Radiation doses are expressed in terms of the energy absorbed per unit weight, which is related to the number of ionizations produced within a tissue. The unit of radiation dose is the gray, measured as joules/kilogram.

A major difference between the various kinds of radiation is the average distance between the ionizing events. Whereas the distance between the ionizing events ranges from a few hundred to a few thousand angstroms for gamma and x-rays, it is only a few angstroms for densely ionizing radiation, such as alpha particles. The linear energy transfer (LET) is a measure of ionization density, and it is expressed in units of electron volts deposited in tissue per micrometer of track length. Although there is a continuous spectrum of LET values among the known radiations, for practical purposes, radiations are divided into two primary groups: low LET radiation, which includes x-rays, gamma rays and beta particles, and high LET radiations, which includes neutrons and alpha particles. For high LET radiation, the amount of energy deposited per track length is very high compared to the distribution of energy for low LET radiation, in which the ionizations are spaced further apart.

Pertinent Radiation Terminology II

- Relative Biological Effectiveness (RBE) is a term used to compare the relative effectiveness of radiations with differing LET values in producing a given biological effect.
- The Quality Factor (Q) is another LET dependent factor which is used to compare the effectiveness of different types of radiation in producing biological effects.



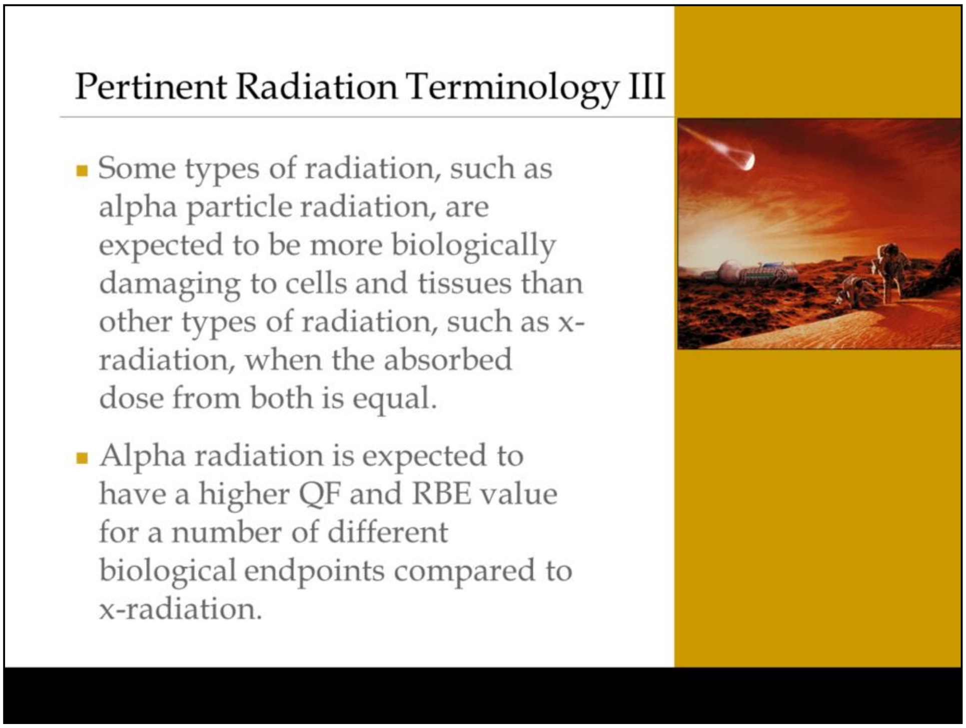
Transcript:

The Relative Biological Effectiveness, the RBE, is a term used to compare biologic effects for different kinds of radiation. RBE is defined as the ratio of the dose required for a given biological effect with x-rays to the dose required for the same effect with the radiation in question. In general, RBE increases with increasing LET for a number of different biologic effects.

The Quality Factor (Q) is used for purposes of radiation protection and is another LET-dependent factor by which doses are multiplied to account for the varying effectiveness of different kinds of radiation. The major unit of radiation dose which accounts for the biological effectiveness of different kinds of radiation is the Sievert.

Image Reference.

NASA. (2000). *Earth's magnetosphere*. Retrieved 06-15-2008 from http://www.nas.nasa.gov/About/Education/SpaceSettlement/designer/magneto.gif



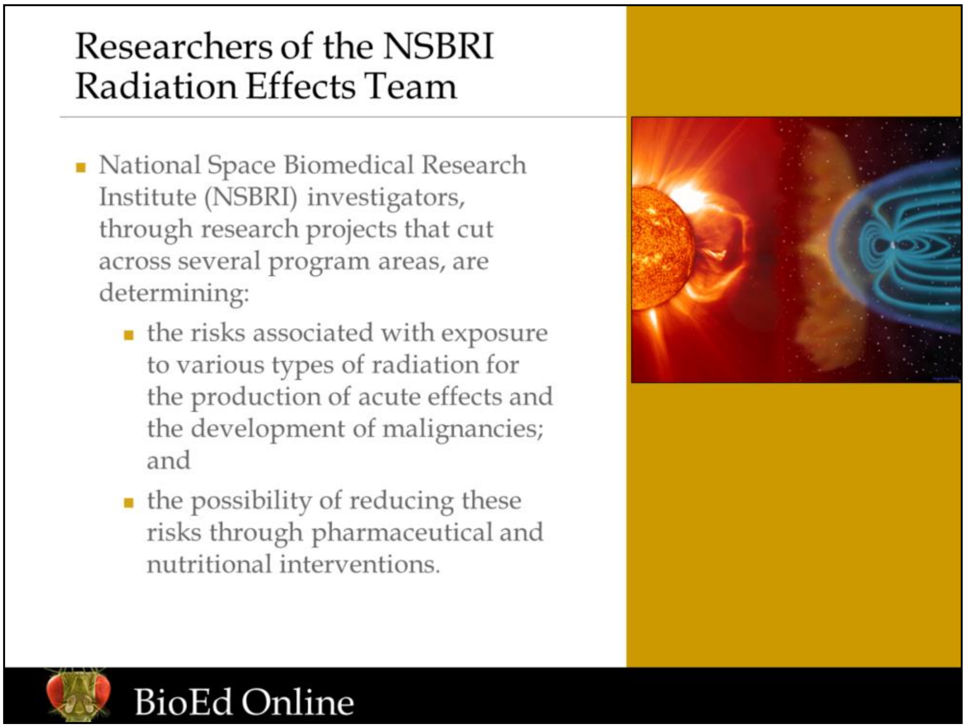
Transcript:

The radiation from HZE particles (heavy charged particles encountered in space) is high LET radiation, with characteristics much like the radiation from alpha particles, to which we are exposed on earth. We are all regularly exposed to relatively low doses of alpha radiation, from sources in our air, food and water. Cigarette smokers are exposed to considerably higher doses of alpha radiation. Alpha particles have very little penetrating ability, as they expend their energy rapidly. For example, a 5-MeV alpha particle, having a range of 35 microns in tissue, will not penetrate below the cornified layer of the skin, and is therefore is not an external hazard. If inhaled or ingested, however, an alpha particle can become hazardous as it may deposit all of its energy within one or two cells. Thus, the amount of local damage can be very great.

Unlike alpha radiation, the radiation from HZE particles has the ability to penetrate deeply into tissue and cause biologic effects in internal organs. HZE particle radiation is thought to be highly effective at inducing cancer and producing other adverse biological effects, as compared to x-rays. RBEs (RBE = relative biological effectiveness) greater than 20 have been observed for the production of some types of tumors in animals by HZE particles, suggesting that a dose of HZE particle radiation can cause more than 20 times as much cancer in animals as the same dose of low LET radiation.

Image Reference.

NASA. (2000). *Mars simulation*. Retrieved 06-15-2008 from http://sohowww.nascom.nasa.gov/gallery/images/sunparts.html

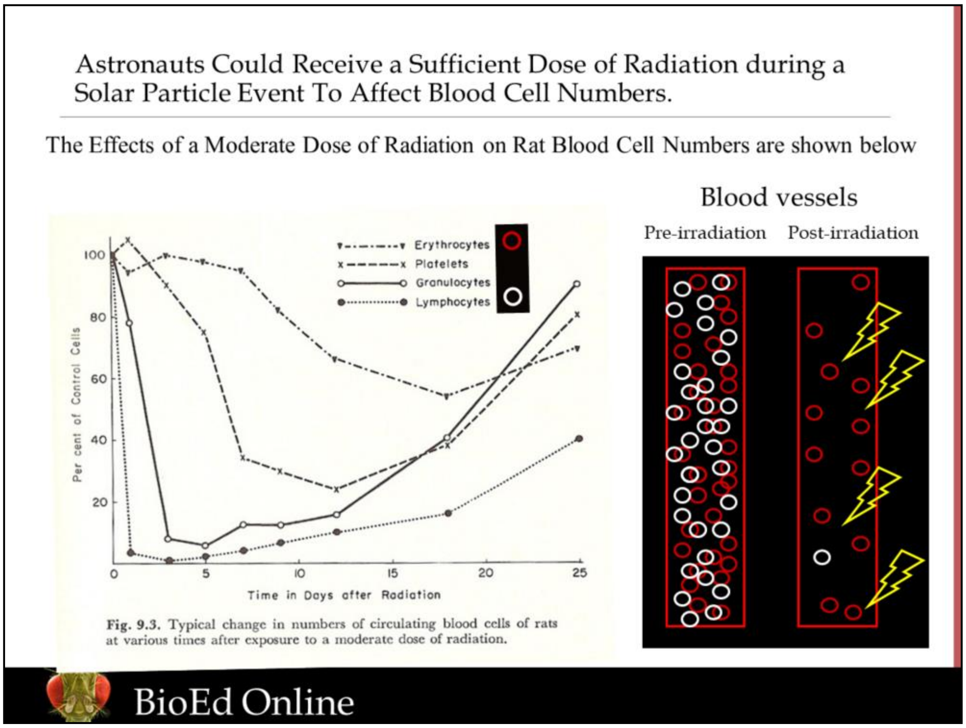


Transcript:

Researchers of the National Space Biomedical Research Institute (NSBRI) Radiation Effects Team are examining risks of various biological effects from exposure to space radiations, and we are attempting to develop countermeasures to reduce the risks associated with exposure to space radiations. What are the radiation risks for space travel? Radiation exposures during space travel may kill cells, weaken the immune system, cause mutations and have other effects that can lead to cancer, cataracts, cardiovascular and central nervous system injuries and other disorders. Through research projects that cut across several program areas, NSBRI investigators are determining 1) the risks associated with various types of radiation for the production of acute effects and the development of malignancies, and 2) whether it is possible to reduce these risks through pharmaceutical and nutritional interventions.

Image Reference:

NASA. (2000). *Sun's magnetic field and releases of plasma*. Retrieved 06-15-2008 from http://sohowww.nascom.nasa.gov/gallery/images/magfield.html



Transcript:

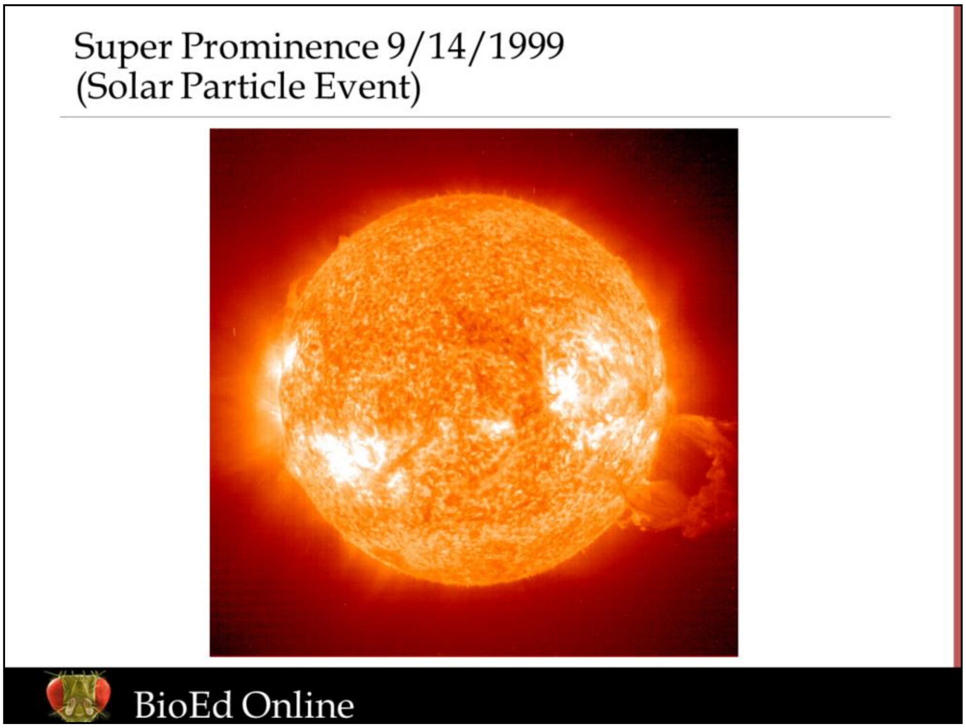
Many of the current NSBRI Radiation Effects Team projects are aimed at assessing risks of space radiation-induced adverse effects, such as those leading to heart disease (cardiovascular risk), cancer and hematological parameters. It is recognized that ionizing radiation has major effects on the cells of the immune and blood-forming systems, with particularly profound effects leading to decreases in the numbers of circulating granulocytes, also called polymorphonuclear leukocytes, and lymphocytes, as can be observed in the graph above, showing the changes with time in numbers of circulating blood cells following exposure to a moderate dose of radiation.

Several current projects involve studies related to the development of pharmaceutical and dietary supplement countermeasures for the cytotoxic effects of space radiation on hematopoietic cells and their progenitor cells, and for the development of space radiation-induced malignancies derived from hematopoietic cells. Another project involves studies of countermeasures for synergism between space radiation and hind limb unloading, an animal model system simulating microgravity conditions, in loss of white cells (lymphocytes).

Image Reference:

Casarett, A.P. (1968). Fig 9.3. *Radiation Biology*. United States Atomic Energy Commission. (Prepared under the direction of the Institute of Biological Science For the Division of Technical Information, United States Atomic Energy Commission), Washington, D.C.

Kennedy, A.R. (2008). *Blood vessels.* Unpublished data.



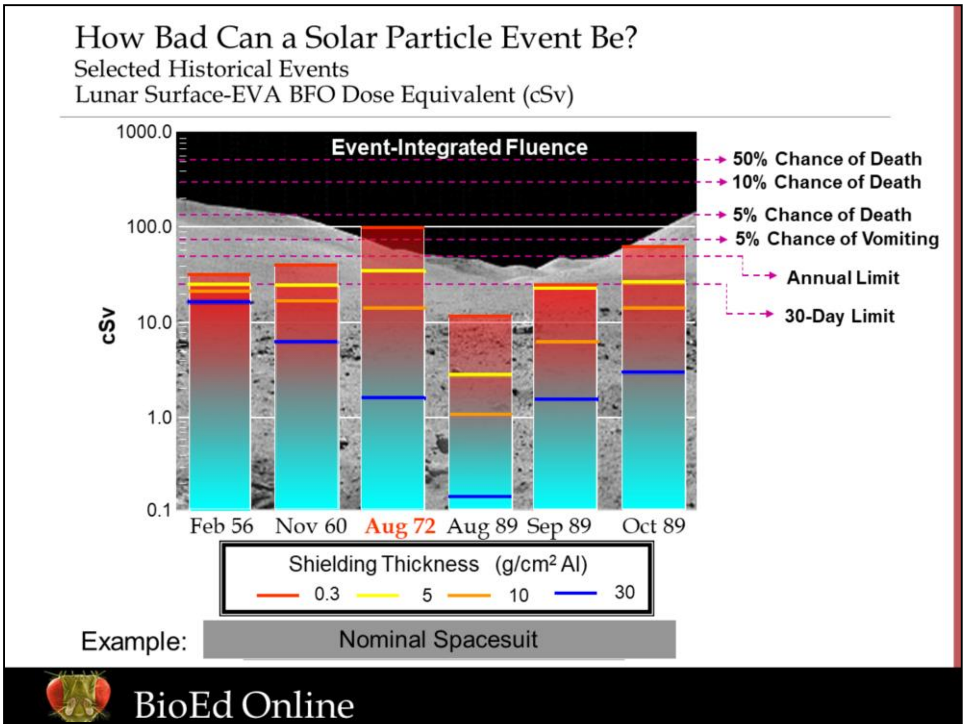
Transcript:

In the future, it is expected that NSBRI’s Radiation Effects Team will be primarily focused on acute effects of high-energy proton radiation of the types and doses which may be encountered during a solar particle event (SPE), the subject of the short movie, produced by Dr. Ron Turner, which you are now seeing. The estimates of doses to be received by astronauts during an SPE vary greatly.

Currently, it is not believed that the doses during an SPE (solar particle event). will be sufficiently high to cause radiation-induced mortality. But the radiation-induced prodromal syndrome (involving nausea, vomiting and fatigue) may occur, along with radiation-induced adverse skin reactions and hematological changes.

Image Reference:

Turner, Ron. *Super Prominence*. By permission.



Transcript:

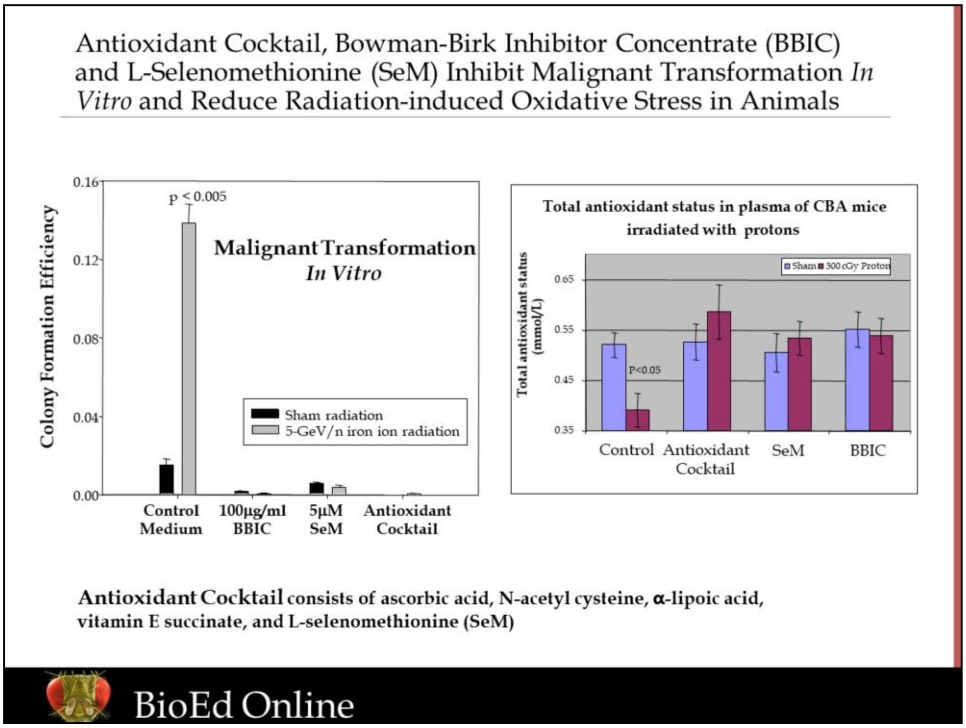
The risks of these effects occurring, and their association with various potential doses of radiation which could be received during an SPE, have been estimated by Dr. Ron Turner. Data from past SPEs have been used to formulate estimations for future SPE events.

The most important radiation risk for current radiation workers on earth and for space travelers has been considered to be the risk of developing cancer. So government regulatory guidelines on dose limits for both of these groups of occupationally exposed people have been based on cancer risk estimates.

Radiation-induced cancer takes a very long time to develop. This is called the latency period, during which a tumor develops. Most radiation-induced cancers take decades to develop, so they will not be observed within the time frame of most missions. However radiation-induced malignancies of blood-forming tissues do not take decades to appear; they can develop within a few years after exposure to radiation. Thus, radiation-induced hematological malignancies, such as leukemia, will be a hazard for space travelers during what are called exploration class missions, which will involve extended periods of time in space.

Image Reference:

Turner, Ron. *How Bad Can a SPE Be*? By permission.



Transcript:

To give you some information about the types of specific research projects conducted by National Space Biomedical Research Institute (NSBRI) researchers, I am going to share some of the data collected on space radiation effects with you. The work of some NSBRI-funded investigators has focused on the development of pharmaceutical and nutritional countermeasures which could be effective at reducing the risks of space radiation-induced malignancies.

Our own work has focused on the development of antioxidant preparations as potential countermeasures for space radiation-related malignancies and other adverse effects caused by space radiation. We have primarily used three different antioxidant preparations in our studies. One of these preparations is L-selenomethionine. While selenomethionine is not an antioxidant itself, it is considered an important part of the antioxidant defense systems in our bodies, as it plays a major role in maintaining the activities of two powerful antioxidant enzymes, known as glutathione peroxidase and thioredoxin reductase. A Recommended Dietary Allowance (RDA) has been established for selenium, a trace element. But it appears that higher levels of selenium than the RDA are necessary for cancer preventive activities. Selenomethionine is an organic form of selenium that has been and is currently being used by the National Cancer Institute in large-scale human cancer prevention trials.

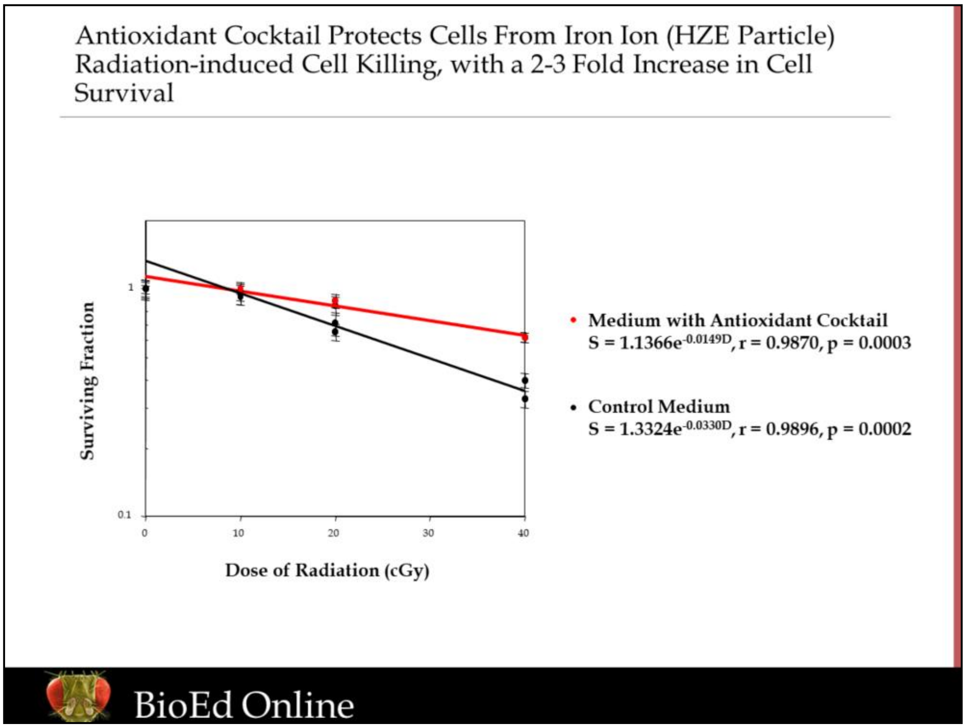
We have also used selenomethionine as part of an antioxidant mixture, containing selenomethionine, vitamins C and E, alpha-lipoic acid, and N-acetyl cysteine. I'm sure you have already heard about the antioxidant properties of vitamins C and E. Alpha-lipoic acid is a potent antioxidant that is both lipid- and water-soluble, and is often considered to be like a B-vitamin. N-acetyl cysteine is a small molecular weight thiol which has antioxidant activity itself. It is also a precursor to intracellular glutathione, a tripeptide small molecular weight thiol that is a versatile and powerful protector against radiation-induced oxidative damage.

We have also used another antioxidant preparation in our studies, which contains the soybean-derived protease inhibitor, known as the Bowman-Birk Inhibitor. Bowman-Birk Inhibitor Concentrate, or BBIC, is the form of BBI utilized in our space studies, as BBIC is the form of BBI which has been used in human trials for well over a decade. Both BBI and BBIC have been shown to protect against numerous radiation-induced biological effects.

As described earlier in this presentation, the important biological effects of many types of radiation are brought about by the ionization of atoms within cells, which in turn can lead to the production of free radicals. As approximately 80% of cells is water, oxygen-based free radicals, known as reactive oxygen species, are thought to be particularly important in the production of biologic effects from many types of radiation. Therefore, it seems reasonable to assume that antioxidants might be able to interact with the radiation-produced free radicals and eliminate or minimize the biological effects produced by radiation exposures. Since antioxidant compounds have very different characteristics (for example, their distribution patterns in the body, solubilities in biologic tissues, abilities to interact with different free radicals, etc.), it might be expected that mixtures of different antioxidant compounds could be more effective than expected for a single antioxidant compound acting by itself.

Image Reference:

Kennedy, Ann. (2007). *Antioxidant Cocktail, Bowman-Birk Inhibitor Concentrate (BBIC) and L-Selenomethionine (SeM) Inhibit Malignant Transformation in vitro and Reduce Radiation-Induced Oxidative Stress in Animals*. Radiation effects. BioEd Online: Houston, Tx.

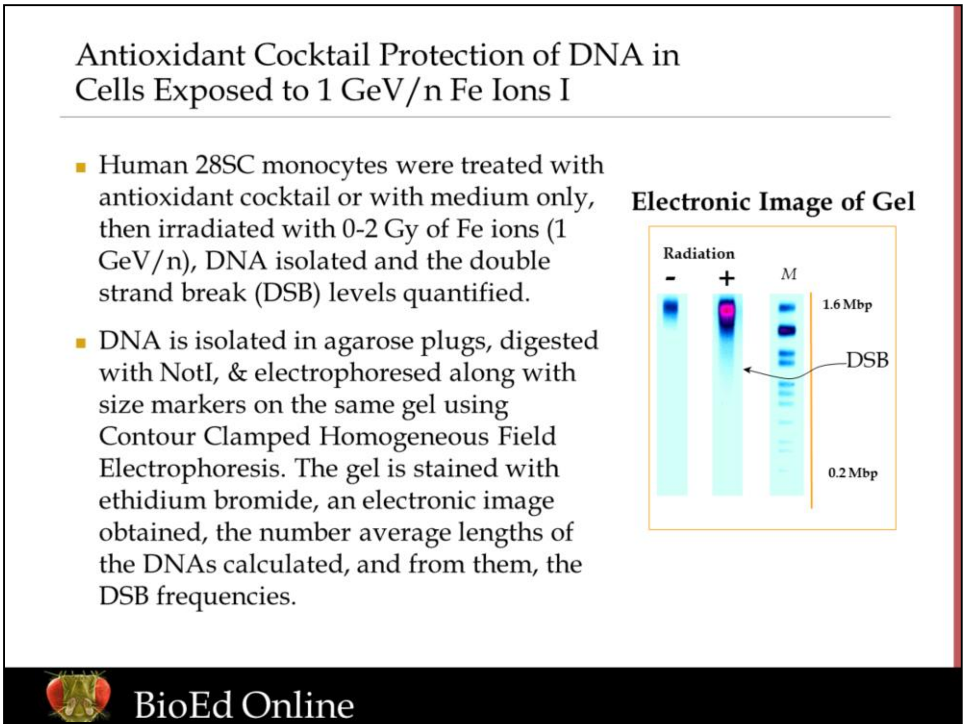


Transcript:

Our work has shown that several different agents, all characterized as dietary supplement agents, can affect space radiation-induced biologic endpoints, including cytotoxicity, the induction of malignant transformation in cells cultured in vitro, and the total antioxidant status of animals, which is a biomarker related to the ability of the animal to handle radiation-induced oxidative stress.

Image Reference:

Kennedy, Ann. (2007). *Antioxidant Cocktail Protects Cells From Iron Ion (HZE Particle) Radiation-induced Cell Killing, with a 2-3 Fold Increase in Cell Survival.* Radiation effects.



Transcript:

In a collaborative study with other National Space Biomedical Research Institute (NSBRI) researchers and members of the Radiation Effects Team, Dr. Alan Gewirtz and Dr. Betsy Sutherland, we observed that an antioxidant mixture (called the antioxidant cocktail in the figures shown here) could reduce the levels of double-strand DNA damage produced in hematopoietic cells by iron ions.

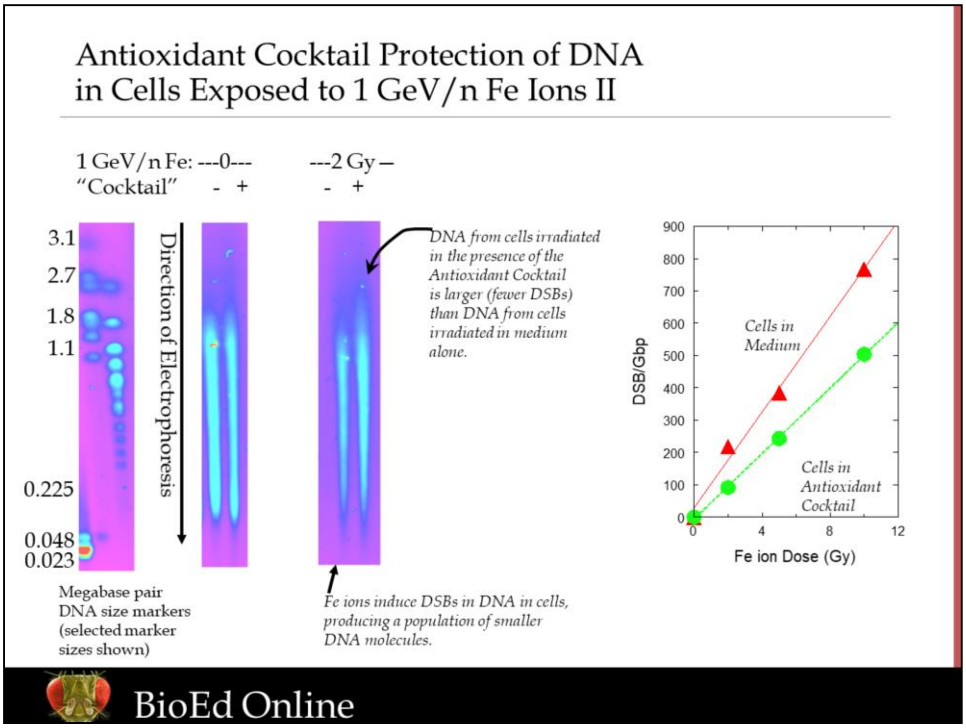
Additional Information:

Gy = Unit of measurement of the absorbed radiation dose (which measures the total energy absorbed per unit mass). A Gray (Gy)_is defined as: 1 Gray (Gy) = 1 Joule/kg. An older unit for the absorbed dose, which is no longer used, is the rad, which is defined as: 1 rad = 100 ergs/g = 0.01 Gy.

GeV = In particle physics, energy is expressed in terms of electron volts (eV). One eV (electron Volt) is the amount of energy an electron acquires when it moves through a potential difference of 1 Volt (in a vacuum). G stands for Giga, or 10^9. Thus, a GeV is a billion electron Volts.

Image Reference:

Kennedy, Ann. (2007). *Antioxidant Cocktail Protection of DNA in Cells Exposed to 1 GeV/n Fe Ions*. Radiation effects. BioEd Online: Houston, Tx.



Transcript:

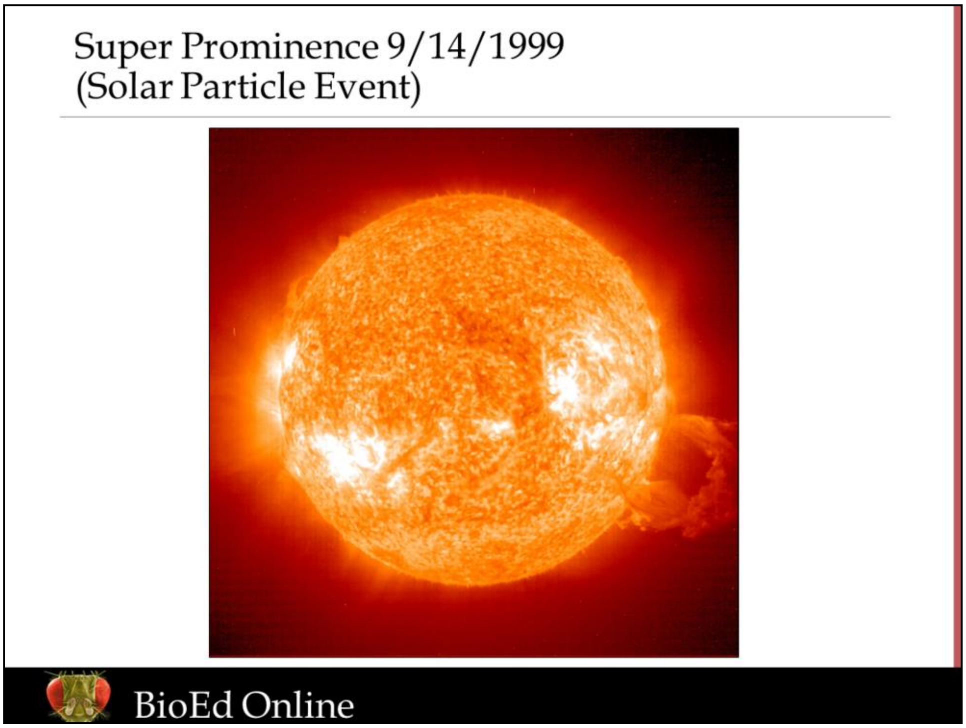
It is generally assumed that radiation-induced double-strand DNA breaks can result in important biologic effects, so a reduction in levels of these DNA lesions would be expected to result in less biologic damage. This is just one example of a collaborative project between National Space Biomedical Research Institute (NSBRI) Radiation Effects Team members. The NSBRI structure encourages such collaborative projects, and there are numerous other examples of collaborative studies within the Radiation Effects Team, between members of the NSBRI Radiation Effects Team and other NSBRI Team members, and between members of the NSBRI Radiation Effects Team and NASA-funded investigators.

At this time, NSBRI investigators have shown that the major space radiation-induced biological effects of concern (that is cell killing, mutation and cancer development) can be prevented or minimized. That is to say, "proof of principle" exists for the potential elimination of space radiation biologic effects, including those produced by HZE particle radiation. It is now clear that there are many different classes of modifying agents; these modifying agents have different potential toxicities and side effects. The challenge for NSBRI researchers now is to determine the best possible combinations of modifying agents so that the potential biological effects from space radiations can be eliminated with the fewest possible toxicities and side effects of the pharmaceutical or nutritional supplement agents utilized.

The investigations of the NSBRI Radiation Effects Team are focused on important research questions of particular relevance to both the NSBRI and NASA. NSBRI researchers will soon be focused on space radiation risks and countermeasures related to the acute effects which may occur as a result of astronaut exposure to proton radiation during an SPE.

Image Reference:

Kennedy, Ann. (2007). *Antioxidant Cocktail Protection of DNA in Cells Exposed to 1 GeV/n Fe Ions.* Radiation effects. BioEd Online: Houston, Tx.



Transcript:

As this is of major importance at this time, I will end our discussion with a photo of a particularly prominent SPE (solar particle event). Hopefully, the astronauts will not be exposed to the major radiation doses expected from such an SPE. As they could be, however, it is hoped that the work of the NSBRI Radiation Effects Team can result in the identification of specific countermeasures that will minimize or prevent the expected biological effects.

Image Reference:

Turner, Ron. *Super Prominence*. By permission.