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# Dose and Dose Rate Effectiveness Factors

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Two large sources of uncertainty in extrapolating from Japanese survivor data to space radiation are dose rate and quality factor. Dose rate requires translation from the instant delivery of radiation from an explosion to a similar dose delivered over days, months, or even years. Quality factors translate the effects observed due mainly to gamma rays from the atomic bomb into the effects predicted from long term exposure to space radiation. Understanding how to achieve these translations requires consideration of the physical constitution of tissues and organs, and an understanding of the time course of their response to radiation injury.

Recall that living organisms consist of atoms, mainly carbon, hydrogen, oxygen and nitrogen. These atoms are not distributed uniformly through the body. Instead, they are combined into molecules of shapes and sizes required to perform all the tasks required by the maintenance of life. The binding of atoms into molecules is done by the atomic electrons who determine the tissue chemistry. The molecules are further organized by being packaged into cells, pouches containing similar combinations of molecules, serving as compartments inside of which the business of life can be conducted.

The sizes of cells are such that approximately 50,000 of them would have to be aligned side by side to cover one inch. Atoms are a hundred thousand times smaller, and the billions of atoms on a DNA molecule have to be twisted into helices several times in order to fit into the cell. Atoms, like tiny solar systems, have electrons circulating around a nucleus that is another hundred thousand times smaller.

The radiation in space consists of high-speed atomic nuclei – atoms that were created with no electrons in their original supernova furnace. Their diameters range from that of a hydrogen nucleus for protons, to about 4 times that size for the heaviest nucleus of biological importance, that of iron. To a first approximation, nuclei consist of protons and neutrons. The protons are charged; each proton has exactly the same charge as an electron, except that it is positive rather than negative. When an atom is fully assembled into an element, the number of electrons is equal to the number of protons, so that the net charge of an atom is zero. Electrons on an uncharged material can be removed by rubbing: if you take a plastic comb and rub it on a piece of cloth, it becomes charged and you can use it to lift small pieces of torn paper (also charged by tearing). This doesn’t work with metal because electrons can move across the atoms of a metal, and quickly compensate for any electrons rubbed off.

The high-speed nuclei in space are basically submicroscopic bullets. They traverse the tissue and organ material and rub against the atoms. If they go very fast, they can knock off one or a few electrons without disturbing the atoms very much, similar to how the bottom checker in a stack of checkers can be removed without disturbing the stack by hitting it with a knife very quickly. The knocked-off electrons can collide with further atoms, and this sequence of reactions can cause collisions far from the path of the incident tiny bullet. The faster the bullet, the further away its effect can thus be felt.

The charge on the tiny bullet nucleus corresponds to its caliber. At any speed, the higher the charge, the more electrons that can be involved in any collision: it is as if one took a thicker object than a knife in the checkers stack experiment. It still works, except maybe more than one bottom piece will be removed.

Overall, the combination of speed and charge determines how much energy will be lost along the track of the nucleus as it burns its tiny hole through the tissues. A highly charged – large caliber – nucleus at a high speed may result in the same energy deposition along the path as that of a smaller caliber nucleus going through more slowly. This is entirely similar to the heat generated by rubbing two surfaces: rubbing two rough surfaces together may heat them up to the same temperature as rubbing two smoother surfaces very fast. The difference will be that the high speed nucleus leaves fewer electrons behind, but they each have more energy and are spread out over a greater distance away from the track, whereas the slower small caliber nucleus will leave a trail with more electrons, but all be concentrated near the track. The total energy deposited along the track, given by the number of electrons times the recoil energy of each one, can be the same.

Once each tiny bullet has gone through, the electrons and atoms start recombining. In those cases where electrons have gone too far, molecules may no longer be held together, leading to effects that range from changes in shape to breaks in large molecules like DNA. If there are large numbers of electrons and atoms with missing electron (“ionized” atoms) recombination can take place more easily than when electrons and ionized atoms are separated by relatively large distances and, therefore, the number of damaged molecules left over after all the recombination has taken place tends to be less after the passage of a slow particle than after the passage of a fast one. The chemical changes are quickly recognized by the cellular machinery, and various processes start to repair the burn hole left behind by the nucleus shooting through. Some of these processes occur almost instantaneously; others may take longer and may depend on the body’s immune system, age, gender, and activity of the tissues involved.

As in any wound, living organisms have multiple healing processes built in and eventually most damage is repaired. In the case of regular burn wounds, caused by fire, scalding with boiling water, or overexposure to the sun, tissues generally heal to the point that a second exposure happens to “naïve” tissue, as if it were the first time, and healing proceeds accordingly. The course of healing can be disrupted in several ways: if the exposure compromises a very large part of one organ, if the exposure affects more than one tissue, and if a second exposure occurs before the damage from the first exposure has fully healed.

With this simple picture in mind, it is easy to visualize the effects of dose, dose rate and radiation quality. Dose is the energy left behind by the total number of nuclei that traverse the body. Slow particles rub harder against atoms, and so leave behind more energy than fast particles. Similarly, large caliber nuclei leave behind more energy than small caliber nuclei. The total number of initially damaged molecules will be proportional to the dose.

Dose rate is the number of nuclei that hit the tissue in a given time. If that time is greater than the time it takes for the tissue to heal, then the second, third, and subsequent nuclei will find healthy tissues and organs, that will have the full repair capability of undisturbed tissue. However, if there is residual damage from a prior particle coming through, the healing process may be more difficult. The dose rate effectiveness will also depend on how many cell in the tissue were disturbed by the passage of either nucleus. If more cells are affected, as they might be, away from the track of a high speed nucleus, the chances of finding a previously disturbed cell are greater. Thus, dose and dose rate effects are not independent.

Close to the track of a passing nucleus, the molecular damage will be related to its caliber, i.e., to its charge. For example, very many atoms along a DNA molecule may have the molecular bonds broken, making the healing process more difficult and more prone to errors. Understanding the effect of nuclear charge on biological outcome is often expressed as Relative Biological Effectiveness (i.e., relative to radiation with well known biological effects, like x-rays).

Prescribed values of the relative effectiveness of radiation, especially for cancer mortality, are used in radiation protection under the name of Quality Factor. To a first approximation, these depend on the energy left behind along the track of a nucleus (technically known as Linear Energy Transfer, or LET): more rubbing, more heat, more damage. At some point, damage to the cells in the path of the bullet is so great that the cell dies, and more LET is wasted on it. Thus, the quality factor for cellular effects rises as the damage increases, and then decreases because the deposited energy is wasted. The process for tissues is slightly more complicated and the quality factor for tissues is not thought to decrease as the LET goes up, but evidence is scant. However, the quality factor will be different for different tissues at a given LET, in the absence of dose rate complications.

The LET changes as the nucleus slows down. If the nucleus slows down too much, it never makes it out of the tissue. This is a problem for experiments and therefore high energy nuclei are the preferred radiation. At the highest energies, nuclei lose relatively little energy, and therefore keep more or less the same velocity and, hence, LET, throughout their path. Such experiments are fundamentally important and are called "track segment irradiations." As we have seen, different combinations of charge and speed can lead to the same LET.

Thus, in order to determine the accuracy of risk predictions for GCR, the following questions need to be answered:

1) What are the rate-determining processes in cellular and tissue repair, and what is their time course?
2) Which of these processes can be affected, and in what way, by the dose rate of exposure to space radiation?
3) What is the quality factor for different tissues at a given LET?
4) How does the quality factor for different tissues at a given LET change as a function of particle charge (caliber)?

Experiments to answer such questions require exposures to different particles at the same LET, over the range of maximal LET changes, for several doses and dose rates bracketing the values obtaining in space. Validation of the models based on the results of the experiments needs to be obtained by comparing their predictions in mixed fields simulating the spectrum of space radiation.