The Use of Biomarkers to Predict Radiation Dose and Risk During Space Flights

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Overview of the Subject

During space flight, careful and complete physical measurements are made to characterize the radiation dose that is received by the astronauts. Biological changes are also evaluated in the astronauts to determine any biological changes induced by radiation during the space flight. Biological evaluations are done both before and after the space flight to ensure that the effects were induced by the space environment. These "biomarkers" have been very useful in validating the radiation doses experienced by the astronauts. There have been efforts to relate the biomarkers of dose to risk and use these changes to suggest levels of risk that the astronauts achieved as the result of the space flight. However, there are difficulties in relating radiation induced biological changes to risk and although many biomarkers are useful predictors of dose, they may not accurately predict excess risk.

Brief History

The use of biodosimetry has a long history. It relates back to radiation accidents where no physical dosimetry was present. Counting the frequency of chromosome aberrations in the blood lymphocytes provides the best method to estimate radiation dose in humans. A summary paper by Bender et al. 1988 provides additional information on the types of aberrations and their use as biomarkers of radiation dose following radiation accidents. It has been widely accepted that the frequency of chromosome aberrations, especially, dicentric chromosome aberrations and micronuclei, provide a very useful and well characterized measure of radiation dose. As technology has improved, additional methods of measuring chromosome aberrations have been developed and proven to be very useful in measuring complex chromosome damage not detected by the older methods. Additional reading on these techniques is available (Loucas and Cronforth 2001, Shi et al. 2012).

Space Radiation

The space environment contains many types of radiation including cosmic radiation with very high energy and mass. During space flight, a number of biomarkers have been used successfully to indicate the radiation dose that the astronauts received (George et al. 2002). This work has been critical since the radiation environment in space contains a wide range of different high energy cosmic radiation that have unique properties and produce unique biological damage that can be detected using biomarkers(George et al. 2003). The gold standard as a marker of radiation dose is chromosome damage – both aberrations (Bender et al. 1988) and micronuclei (Brooks et al. 2003). Many other biomarkers of radiation dose have shown promise. Additional

information is available on some of these biomarkers of radiation dose including changes in gene expression (Amundson et al. 2000), protein expression and post-translational modifications (Yang et al. 2012) and radiation-induced changes in metabolic profile (Hu et al. 2012).

Another concern with the use of biomarkers is relating the biological change to significant changes in radiation risk. There are biomarkers of exposure and dose as well as markers of genetic sensitivity and finally the biological changes that result from the development of diseases, especially cancer. Additional reading is available on classification of biomarkers of exposure, sensitivity and disease (Brooks 1999). Other classifications of biomarkers have been generated and have found many uses in medicine. For example, biomarkers would be useful to triage people after nuclear accidents or nuclear war to determine which individuals need and do not need medical attention (Blakely et al. 2005, Vaurijoux et al. 2009). Such biomarkers would be very critical in determining the necessary medical treatment. Some of the population exposed to high doses may require treatment, while those with low dose exposure may need to be reassured that they do not require medical treatment. Also, biomarkers would be essential in assessing probability of causation for later health effects for which legal redress may be sought.

Biomarkers of Radiation Risk

A major concern is whether radiation- induced changes in biomarkers accurately predict radiation risk. Since risk has been shown to change as a function of radiation dose and biomarkers predict radiation dose, it has been suggested that biomarkers, especially increases in chromosome damage, can predict radiation-induced cancer risk.

Some research suggests that biomarkers of dose do not reflect this risk. For example, some tissues are sensitive to radiation-induced cancer, while others show little cancer following radiation exposure. In the rat, radon (radon and its daughter products) produced a marked increase in lung cancer, while in the same thousands of rats exposed to radon, there was no increase in tracheal cancer. The frequency of radon-induced chromosome aberrations in the radiation- resistant trachea was not different from the frequency of aberrations induced in the deep lung fibroblasts (Bao et al. 1997) or epithelial cells (Brooks et al. 1997), both of which are involved in lung cancer. There are also species differences in the sensitivity to radon-induced lung cancer. The Wistar rat has a very high frequency of radon-induced lung cancer, while the Chinese and Syrian hamster show no increase in lung cancer following radon inhalation. Interestingly, when the frequency of micronuclei was measured in these different species, the Wistar rat, with the highest cancer rate, had a lower frequency of micronuclei and DNA damage than either the Chinese or Syrian hamster (Khan et al. 1995). These aberrations were retained in the cell population of all three species for a similar length of time which should suggest similar potential for increased radiation-induced lung cancer, yet cancer rates were different. Finally, it is well-established in human populations that there are marked differences between individual sensitivity to the induction of cancer. Most biomarkers do not reflect these differences, again suggesting that many biomarkers reflect changes in dose and not cancer risk.

Additional information on the role that the biomarkers play in risk from space flight is available and was published by the National Council on Radiation Protection and Measurements (NCRP

Report No. 167) "Potential impact of individual genetic susceptibility and previous radiation exposure on radiation risk for astronauts" as a report (NCRP 2010).

The experimental evidence presented here suggests that many biomarkers are good predictors of radiation exposure and dose. However, because of biological variability between individuals, tissues and species, many of the biomarkers do not predict radiation risk. The presence of aberrations from radiation exposure, especially at low doses, doesn't mean that individual risks has been increased. Much research on biomarkers of space radiation has provided very good characterization and measurement of the radiation dose delivered during space missions. Still, additional research is required to link these biomarkers to radiation-related changes in cancer risk.

References

Amundson, S.A. Do, K.T. Shahab, S. Bittner, M. Meltzer, P. Trent, J. Fornace A.J. (2000) Identification of potential mRNA biomarkers in peripheral blood lymphocytes for human exposure to ionizing radiation. Radiat. Res. 154, 342-346.

Bao, S., P.W. Harwood, W. B. Chrisler, K.M. Groch, A.L. Brooks (1997) Comparative Clastogenic Sensitivity of Respiratory Tract Cells to Gamma Rays. Radiat. Res. 148, 90-97.

Bender, M.A., A.A. Awa, A.L. Brooks, H.J.Evans, P.G. Groer, L.G. Littlefield, C. Perira, R.J. Preston, B.W. Wachholz (1988) Current status of cytogenetic procedures to detect and quantify previous exposures to radiation, Mutation Res. 196,103-159.

Blakely, W.F. Salter C.A. Prasanna, P.G. (2005) Early-response biological dosimeter-recommended countermeasure enhancements for mass-casualty radiological incidents and terrorism, Health Physics 89 (5), 494-504 Health Physics 89 (5), 494-504.

Brooks, A.L. (1999) Biomarkers of exposure, sensitivity and disease, International Journal of Radiation Biology 75, No 2. 1481-1503.

Brooks, A.L., S. Bao, P.W. Harwood, B.H. Wood, W.B. Chrisler, R.A. Gies, F.T. Cross (1997) Induction of Micronuclei in Respiratory Tract following Radon Inhalation. Inter. J. Radiat. Biol. 72, No.5 485-495.

Brooks, A.L., Lei, X.C. and Rithidech, K. (2003) Changes in biomarkers from space radiation may reflect dose not risk. Advances in Space Research 31: 1505-1512.

George, K, Durante, M. Willingham, V. Wu, H. Yang, T.C. Cucinotta, F.A. (2003) Biological effectiveness of accelerated particles for the induction of chromosome damage measured in metaphase and interphase human lymphocytes. Radiat. Res. 160, 425-435.

George, K, Wu, H. Willingham, V. Cucinatta, F.A. (2002) Analysis of complex-type chromosome exchanges in astronauts lymphocytes after space flight as a biomarker of high-LET exposure, J Radiat. Res 43 Suppl S129-S132.

Hu, Z.P. Kim, Y.M., Sowa, M.B. Robinson, R.J. Gao, X. Metz, T.O., Morgan, W.F. Zhang, Q. (2012) Metabolomic response to human skin tissue to low dose ionizing radiation, Mol. Biosyst 2012, 8, 1979-1986.

Khan, M.A., F.T. Cross, R.L. Bushbom, A.L. Brooks (1995) Inhaled radon-induced genotoxicity in Wistar rat, Syrian hamster and Chinese hamster deep-lung fibroblasts *in vivo*. Mutat. Res. 334, 131-137.

Loucas, B.D. and Cornforth, M.N. (2001) Complex chromosome exchanges induced by gamma rays in human lymphocytes: a mFISH study. Radiat. Res. 155, 660-671.

NCRP (2010). National Council for Radiation Protection and Measurements, *The potential Impact of Individual Genetic Susceptibility and Previous Radiation Exposure on Radiation Risk for Astronauts.* NCRP Report No. 167 (National Council for Radiation Protection and Measurements Bethesda MD).

Shi, L. Fujioka, K. Sun, J. Kinomura, A. Inaba, T. Ikura, T. Ohtaki, M. Yoshida, M. Kodama, Y. Livingston, G.K. Kamiya, K. Tashiro, S. (2012) A modified system for analyzing ionizing radiation-induced chromosome abnormalities. Radiat. Res. 177(5), 533-538.

Vaurijoux, A. Gruel, G. Pouzoulet, F. Gregore, E. Martin, C. Roch-Lefevre, Voisin, P. Vosin, P., Roy L. (2009) Strategy for population triage based on dicentric analysis. Radiat. Res. 171,541-548.

Yang, F., Waters, K.M. Webb-Robertson, B.J. Sowa M.B. von Neubeck, C. Aldrich, J.T. Markillie, L.M. Wirgau, R.M. Gritsenko, M.A., Shao, R. Camp D.G. Stenoien D.L. (2012) Quantitative phosphoproteomics identifies filaggrin and other targets of ionizing radiation in a human skin model. Exp. Dermatol. 21(5), 352-357.