An Introductory Overview of the Epidemiological Study on the Population at the High Background Radiation Areas in Yangjiang, China

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The epidemiological study on the residents of the high background radiation areas in Yangjiang, China was started by Chinese scientists in 1972 and continued until 1986. In 1991, Japanese scientists recognized the importance of the work and a joint feasibility study was conducted with revised protocols. The feasibility study matured to a cooperative project involving both Chinese and Japanese scientists in 1992, which currently is still in progress. The project was divided into three phases; the first being from 1992 to 1995, the second from 1995–1998 and the third from 1998 to 2001. The results of the first phase were reported previously in 1996. The present paper is a historical overview of the studies before the cooperation and the first two phases. Remarks are made on the detailed data on dosimetry, cytogenetic studies and cancer epidemiology of a series of the papers in this supplemental issue. Some problems such as paradoxical observations between cytogenetic results and cancer mortality, and the importance of the high background study in risk assessment are discussed.

INTRODUCTION

In 1972, the High Background Radiation Research Group chaired by Wei Luxin began a health survey in the high background radiation areas (HBRA) in Yangjiang of Guangdong province and neighboring control areas (CA). The purpose of this investigation was to provide some information for evaluating whether any detrimental effects exists in a population experiencing the life long exposure to low dose rate radiation in addition to exposures to preceding generations. Cancer mortality from 1970 to 1974 was reported in “Science” in 1980¹ which attracted the interests of Japanese scientists. Personal cooperation between Chinese and Japanese scientists has continued since then, and the report on further studies was published in a journal, Radiation Biology Research Communication, published in Japan².

Studies by Chinese scientists continued until 1989 extending the survey of cancer mortality

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until 1986\textsuperscript{3}) but it was discontinued since then because of the shortage of research funds. In 1990, based on a proposal by Chinese scientists, possible cooperation including financial support was discussed between Japanese and Chinese scientists. In January 1991, an expert review meeting was held in Kyoto supported by the Health Research Foundation to examine the past research and to propose revised methods and protocols for the better estimation of radiation risks of the low dose continuous exposure. Based on the recommendations of the review meeting, a feasibility study was carried out for one year in 1991 in Beijing and Guangdong with the collaboration of Chinese and Japanese scientists.

From 1992 to 1998 the China-Japan cooperative epidemiological study of the high background radiation areas was carried out using the revised protocol as summarized in this paper.

**PREVIOUS STUDIES ON CANCER MORTALITY**

The first paper on this high background radiation area was published in “Science” in 1980\textsuperscript{1}). Concerning cancer mortality, a retrospective 5-year survey was carried out from 1970 to 1974. The information was collected from the demographic survey and hospital records. Person-year and standardized mortality were $96,533$ and $45.69/10^5$ in the high background radiation area (HBRA), and $122,554$ and $44.83/10^5$ in the control areas (CA).

Since then, the health survey has been extended four times by the Chinese scientists; the first for the period of 1975–1977, the second for 1978–1981, the third for 1982–1984 and the fourth for 1985–86. Combined reports were published in 1996 by Wei et al by Atomic Energy Press, Beijing, China\textsuperscript{3}). A summary report was published in “Journal of Radiation Research” in 1990\textsuperscript{4}). Person-years and age- and sex-adjusted cancer mortality per $10^5$ person-year from 1970 to 1986 were $1,008,769$, and $48.81$ in HBRA, and $995,070$ and $51.09$ in CA. Thus, the cancer mortality did not differ significantly between HBRA and CA. However, when an analysis was made on the population of 40–70 year olds, the solid cancer mortality of HBRA was significantly lower than that of CA; $143.8$ in HBRA and $168.0$ in CA, $p = 0.04$.

In 1979, a cancer registry system was introduced in the investigated area in which local physicians, with the help of section hospitals, county hospitals and many health administrative organizations, reported all cancer cases and cancer deaths to the registry. Diagnoses were examined carefully, sometimes re-examined and confirmed by an expert group who met at the investigated areas to evaluate cases twice a year. Meanwhile, death from all causes were also registered and analyzed. Thus the quality of diagnosis before and after 1979 are different.

**CHINA-JAPAN COOPERATIVE STUDY FROM 1992 TO 1998**

In January 1991 an expert meeting from China and Japan was held to discuss the feasibility of a cooperative epidemiological study on HBRA. Revised protocols for dosimetry, cytogenetic study and cancer epidemiology were proposed. In 1991, a site visit was made by Japanese scientists to Beijing and the Guangdong area to further revise the protocols. The cooperative study
began in 1992 with the new protocols. Major points of the new protocols include the improved dosimetric system for personal dose of the residents, the new cytogenetic technique developed at the National Institute of Radiological Sciences in Chiba, Japan, the improved method of cancer detection and diagnosis together with the shift from geographical to cohort study on three dose groups in HBRA.

In May 1995 a workshop was held in Kyoto to review the results obtained with five Europe-American scientists and five Japanese scientists as consultants. The recommendation was made at the workshop to further improve the research protocols. The following emphases were made in the recommendation: a) to reevaluate the doses to avoid the overlapping of dose levels among the three dose groups, b) to measure Radon and decay products in the environment, c) to study the frequency of stable chromosome aberrations and d) to undertake case-control studies to analyze confounding factors. These recommendations were well incorporated in the second phase of the study of 1995 to 1998.

In the first phase, a cancer survey of the present study was conducted from 1987 to 1990 retrospectively. The results were reported at the International Conference on High Level of Natural Radiation5–14 held in October, 1996, together with the previous results obtained by Chinese scientists. Four sub-population sizes of the cohorts, one in CA and three in HBRA (low, medial and high) were 27,903 and 78,614 (26,093, 28,803, and 23,718), respectively. By expanding the mortality survey from 1979 to 1990 in the previous report to 1995 in the present report, the person-year for CA and HBRA is now increased from 295,572 to 452,011 and from 7990,582 to 1,246,340, respectively. Accordingly, the previous value of 0.99 (0.86–1.14) for the age- and sex-adjusted relative risk (RR) and the 90% confidence interval for all cancer mortality in HBRA, came to be 0.99 (0.89–1.11). Thus, improvement of the confidence interval is attained by expanding the survey length. Similarly, statistical precision for all cancer mortality increased from 73.9 to 87.5 ( for $\alpha = 0.05$, RR = 1.2).

The results reported in the succeeding papers came from these analyses. Details are reported in a series of papers in this issue by specialists on dosimetry, cancer epidemiology and cytogenetic studies. Individual external dose assessments of the inhabitants are reported by Morishima et al15). Internal exposure to Rn and its decay products are assessed by Yuan et al16). Analysis of cancer mortality is reported by Tao et al17). These results are used for risk analysis by Sun et al18). A case-control study on nasopharyngeal cancers is reported by Zou et al19). Cytogenetic analysis was confined to unstable aberrations only in the first phase as reported by Jiang et al20), but was extended to stable aberrations in the second phase as reported by Hayata et al in this series21).

**DISCUSSION**

The third phase of the project is now under way (1998 to 2001) to increase the statistical precision of the epidemiological study further by extending person-years. In parallel with this, more detailed analyses of internal exposures and stable chromosome aberrations on a larger number of residents are in progress. In the following sections, implications of HBRA study to radiation protection and radiation carcinogenesis are discussed.
Studies on natural high level of radiation reviewed in textbooks and UNSCEAR reports

A standard textbook on radiation biology “Radiobiology for the Radiologist” by E. Hall has a section on Areas of High Natural Background Radiation in its fourth edition published in 1994. There, coastal areas in Brazil, a part of France in the Burgundy wine growing district, Njue Island in the Pacific, Kerala in India and the northern Nile delta in Egypt are described as examples of high natural radiation background areas but not Yangjiang, China. The book concluded that it is an important and significant fact that human populations who have lived for generations at levels of background radiation that differ by an order of magnitude show no noticeable difference in the incidence of cancer and genetic disorders.

Contrary to this, Annex A of the UNSCEAR report, “Epidemiological Studies of Radiation Carcinogenesis”, published in the same year of 1994, referred only to the Chinese studies on high background radiation areas in Yangjiang in its section on exposure to natural background radiation. The reports include only studies carried out before the China-Japan cooperation, i.e., mortality study from 1970 to 1986 and a comparison between high and control background radiation areas. Since we have reported preliminary results in the proceedings of the Fourth International Conference on High Levels of Natural Radiation, they will be included in the next report of UNSCEAR.

As for epidemiological studies on populations living in high background radiation areas, very limited reports have been available so far although there are many high background radiation areas in the world as reviewed by Sohrabi. The present study is the most advanced among the similar studies, since it is a cohort study with analyses on dose responses and on confounding factors.

Role of negative data in risk analysis

When we obtained a relative risk below 1 such as in the present studies of RR = 0.99 for all cancers and ERR (excess relative risk) = –0.11%/10mSv for all cancer minus leukemias, their confidence intervals were usually discussed. When the intervals overlap with those of atomic bomb survivors, the data are denounced as not significant. ERR/Sv in HBRA(1979–1995) is –0.10(–0.67,0.69) and that of A-bomb survivors (1950–1990) 0.53(0.43,0.64). The numbers in parenthesis show the 95% confidence intervals. To reduce this confidence interval the cancer survey has been continued to increase person-year as much as possible. Analysis of this study would give more information on the risk of very low dose radiation when combined with the studies on nuclear facility workers who have been exposed to radiation of similar dose ranges.

Usefulness of the personal dosimetry system for studies on radioactively contaminated areas

At the beginning of this study only the geographical mean of field dose was used but after realizing a large difference in gamma-ray dose among houses, various personal dosimetry and model systems have been developed (Morishima et al in this series; see also Wei and Yuan). In many studies on contaminated areas with radioactive fallout a difference between indoor and outdoor doses may be expected. The same methodology will be available there as well. But in natural high background radiation areas we can repeat the measurement and compare the result obtained to confirm the estimated dose. Thus we can conclude as mentioned in the title.
The role of chromosome aberrations in carcinogenesis; is radiation carcinogenesis a direct or indirect process?

Methods of chromosome analysis of peripheral lymphocytes have been well established\(^2\text{4}\). But its relationship to carcinogenesis remains to be elucidated.

As shown by Jiang and others in this series\(^2\text{0}\), unstable chromosome aberrations in lymphocytes in peripheral blood increased by age in proportion to dose rate in the high background radiation areas. Contrary to this, Hayata et al\(^2\text{1}\) have shown that there was no increase in the stable aberrations in the areas. The epidemiological study on cancer mortality in the same area by Tao and others\(^1\text{7}\) have revealed no increase in cancer mortality either. The reason for these contradictory results between chromosome damage and cancer remains to be elucidated. Our tentative explanation is that cancer induction by radiation may not result directly from DNA damage induced by radiation but may result indirectly from radiation-induced genomic instability. Chromosome aberrations that we observed may be directly related to radiation exposure but may not be related to cancer directly. Further detailed analysis of the processes is now in progress.

Is there any adaptive response in HBRA?

Immune function of the inhabitants in HBRA and CA was studied in 1979 and 1982 which showed that the reactivity of the lymphocytes of peripheral blood to in vitro stimulation with PHA was upregulated and the level of unscheduled DNA synthesis of the lymphocytes was found to be higher in the blood samples from the inhabitants of HBRA\(^2\text{5}\). In 1996, another experiment was carried out to explore the possibility of high background radiation inducing a cytogenetic adaptive response in human body\(^2\text{6}\). The results show that long term exposure to low dose from higher natural background radiation may cause human lymphocytes to be less susceptible to subsequent high dose irradiation in vitro\(^2\text{7}\).

CONCLUSION AND PERSPECTIVES

This is the report on Japan-China cooperative study on the high background areas in Yangjiang of Guangdong, China from January, 1991 to March, 1998. A part of the study has been reported previously. A series of papers will cover the detailed results thus far obtained. An epidemiological study on low dose exposure has many difficulties resulting from various kinds of errors. The dose estimation and cancer mortality survey have been carried out after crucial discussion within the research group as well as with outside scientists of the field. The study will be continued for another years to extend person-years as much as possible.

Epidemiological studies on other areas of high background radiation such as Kerala in India and many high radon areas in Europe are in progress. These studies would contribute to a better understanding of the effects of low dose radiation on human health.
REFERENCES