International Radiation Information Center

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This center was re-established in June 1994 in order to reorganize and expand the facilities of Data and Specimens Center of the Atomic Bomb Disaster. Newly reorganized center supports each division of the RIRBM and other institutes through its collection and analysis of international radiation information, and redistributes these information to scientists on a worldwide basis. The center consists of three divisions. They are the Repository of Atomic Bomb Data and Specimens, the International Center for Radiation Survivors, and the Center for Invitation of Foreign Scientists. In April 2002, our institute re-started on new organization plan. We continued to the same projects for research and service continues, our main research fields are as follows;

 (a) Research on collection, arrangement, preservation, and analysis of data and specimens from A-bomb disaster victims. (Reassessment of A-bomb dose at Hiroshima and Nagasaki, and others)

- 368 -
- (b) Collection of information, on worldwide radioactive contamination and its analysis. (Estimation of radiation doses to residents around Chernobyl, Semipalatinsk and Chelyabinsk, and study of diseases caused by the radiation and underlying mechanisms, examination of the actual conditions of the radiation exposed residents in Semipalatinsk by the questionnaire method)
- (c) Biological effects of high LET radiation, e. g. neutrons, and studies of the mechanism of its influence.
- (d) Promotion of international cooperative studies and organizing international symposium on radiation effects.
- (e) Public program of radiation information, and education and training of radiation medical workers.
- (f) Dosimetry and medical assistance in radiation emergency medicine.

Dr. Satoru Endo was appointed to associate professor on April 1, 2004. Dr. Yuka Harada was appointed to research associate on May 1, 2004.

Prof. Masaharu Hoshi acts as the following members:

a member of the permanent secretary and editorial staff of the Journal of the Japan Radiation Research Society, a councilor, a director, an editorial staff, and a member of radiation protection committee of Japan Association of Medical Physics. Further, he is a section manager of Japan Radiological Society, a member of the investigative committee and the betterment of domestic society (JICA) for the Health Care and System of Semipalatinsk, an advisor of Hiroshima-Semipalatinsk Project, and a member of an investigative committee for an urgent countermeasure of Nuclear Safety Commission of Japan, a member of The U. N. science committee domestic correspondence committee, a member of Low Dose of Biological Effects in Central Research Institute of Electric Power Industry, a lecturer in regional forum in Nuclear Safety Research Association, a secretary and a member of the working group, and a member of the home page working group of Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), and a member of Special committee on Nuclear Safety Research, a member of Technology and Science Council of Japan Core Science General Research Connection Committee, Japan Radiological Society councilor, The Science Council of Japan Core Science General Research Connection Committee, Japan Radiological Society of Japan and so forth. Prof. Hoshi has been admitted as an Exemplary Worker of the Health Care System of Kazakhstan for special deserves in the Affair of the Health Care System of the population of Kazakhstan since January 6, 2004.

Dr. Ryungsa Kim is a councilor of the Japanese Society of Chemotherapy. Research Associate, Dr. Satoru Endo is a member of editorial staff of Japan Radiological Society, Noriyuki Kawano is an advisor of Hiroshima-Semipalatinsk Project.

The programs of international symposiums and workshops organized or supported by us are shown in Appendix 1. 3rd Dosimetry Workshop on the Semipalatinsk Nuclear Test Site Area with 10th Hiroshima International Symposium "International intercomparison of radiation dose estimation near Semipalatinsk nuclear test site -For the dose estimation in Dolon village-"on March 9 - 11, 2005 was planned by International Radiation Information Center, and was held by Research Institute for Radiation Biology and Medicine, Hiroshima University. We have been to Semipalatinsk to collect brick samples for the evaluation of external exposure and contamination of soil samples and succeeded in bringing back about 29.3kg of the samples in addition to that obtained in 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, and from November 9 to 17, 2004. For this project, we accepted aid from "Grant-in-Aid for Scientific Research" of the Ministry of Education, Culture, Sports, Science, and Technology. We are measuring these samples now. Similarly, we are performing the study of the effects of radiation for the children living near the Chernobyl Nuclear Power Plant. The project was supported by Sasakawa Memorial Health Foundation and ended in April 1996. However, similar project will be continued mainly in Russia. We have been Semipalatinsk to explore

the realities of *Hibakusha* in Semipalatinsk in terms of the questionnaires and the witnesses. It is possible to clarify their life environment and health condition by means of the questionnaires. The witnesses will show their suffering. Finally, we compare the realities of *Hibakusha* in Semipalatinsk with those in Hiroshima and Nagasaki. By this comparison, radiation effects on *Hibakusha* will be more clear.

1 . Effects of radiation for residents near Semipalatinsk nuclear test site

Hoshi, M., Endo, S., Takada, J.^{*1}, Tanaka, K., Kawano, N., Taooka, Y.^{*2}, Kim, R., Nitta, Y., Telewhan, E., Okamoto, T.^{*3}, Takeichi, N.^{*4}, Yamada, H., Stepanenko, V.^{*5}, Ivannikov, A.^{*5}, Hayakawa, N.^{*6}, Kimura, A.^{*7}, Yamamoto, M.^{*8}, Nailya Chaizhunusova^{*9}, Kazbek Apsalikov^{*9}, Gusev, B.^{*9}, Teleuov, M^{*10}, Zhumadilov, Zh.^{*10}, Katayama, H.^{*11} and Toyota, A.^{*12} (^{*1}Sapporo Medical University, ^{*2}Matsuda Hospital, ^{*3}Grad. Sch. Biomed. Sci., ^{*4}Takeichi Hiroshima Thyroid Medical Clinic, ^{*5}MRRC RAMS, ^{*6}Dept. Epidemiol., ^{*7}Dept. Hematol. Oncol., ^{*8}Kanazawa Univ., ^{*9}Kazakh Scientific Res. Inst. Radiat. Med. Ecology, ^{*10}Semipalatinsk Medical Academy, ^{*11}RERF, ^{*12}Okayama Univ. Sci.)

It is estimated that there are about 500,000 of residents who were exposed by radiations due to nuclear bomb tests at Semipalatinsk nuclear test site. According to journalism, such radiation effects were very hard. However, there are no scientific reports concerning them. In this study, exposed doses for these people will be estimated separately by internal and external exposures. After this estimation thyroid and hematological diseases were examined along with epidemiological studies to verify whether the diseases are due to radiation. The differences between them and Hiroshima and Nagasaki will be considered also.

2 . Evaluation of Hiroshima atomic (A-bomb) dose

Hoshi, M., Endo, S., Takada, J.⁻¹, Tanaka, K., Hiraoka, M., Hayakawa, N.⁻², Shizuma, K.⁻³, Iwatani, K.⁻⁴, Hasai, H.⁻⁵, Oka, T.⁺⁶, Fujita, S.⁺⁷ and Cullings, H.⁺⁷ (⁺¹Sapporo Medical University, ⁺²Dept. Epidemiol. Social Med., ⁺³Grad. Sch. Eng., ⁺⁴Hiroshima Pref. Colleg. Health Welfare, ⁺⁵Hiroshima Kokusai Gakuin Univ., ⁺⁶Kure Univ., ⁺⁷RERF)

Hiroshima atomic bomb (A-bomb) doses of neutrons and gamma rays have been evaluated. Processes of the evaluations are (1) collection of A-bomb irradiated rocks, roof tiles and etc., and measurements of neutron induced radioactivities, such as ¹⁵²Eu Neutron doses of the Hiroshima A-bomb will be evaluated from the measured values of these radioactivities. (2) comparison of the experimental results and the oretical values calculated by a computer code MCNP. In addition to these, we are simulating A-bomb irradiation using the ²⁵²Cf fission neutron source and comparing with the experimentally obtained activity yields in the irradiated material and theoretically calculated yields of them. We are planning to evaluate DS86 dose from (1) and (2). Concerning these studies, we are performing collaboration with U. S. groups and with those of Kyoto University and Nara University of Education.

3 . Dosimetry study of ultrasoft X rays

Hoshi, M., Endo, S., Tanaka, K. and Sasaki, M.^{*} (^{*}Kyoto Univ.)

Energy region of ultrasoft X rays are usually determined to be below 5 keV. These X rays have larger relative biological effectiveness (RBE) for biological materials than those from conventional X ray apparatus or gamma rays, and are considered to have different mechanisms in the induction of biological damages in cells.

Geometrical area of the energy deposition caused by a single absorption of the X rays is as small as the sizes of the DNA double strands. Therefore, the ultrasoft X rays are unique tools to study correlation between physical and chemicalinitial processes induced by ionizations and following biological damage inductions. Such a study of the mechanisms inducing biological damages according to radiation exposures is also useful for the study using neutrons from the neutron irradiator and the ²⁵²Cf source. The explanation should include all of these radiations. At Radiation Biology Center, Kyoto University,

effects of absorption of ultrasoft X rays in culture cells have been studied.

4 . Development of "Monochromatic Energy Neutron Irradiator for Radiobiology Studies"

Hoshi, M., Endo, S., Tanaka, K., Takeoka, S., Kitagawa, K. and Suga, S. (Radiat. Res. Centr. Frontier Sci.)

Monochromatic Energy Neutron Irradiator for Radiobiology Studies (HIRRAC) was installed in this institution. The system consists of an accelerator (3MeV, 1mA, Schenkel type) and three target chambers (Li,Be,³H) for neutron generation and a PIXE target chamber. The accelerator and the two Li (for level and vertical irradiations), the ³H and the PIXE target chambers were constructed in the ²⁵²Cf irradiation room. Neutrons were mainly produced by the ⁷Li(p,n)⁷Be reaction. The production of neutrons was tested and the neutron dose rates measured by using twin chambers were verified to be more than planned one (30 cGy/min at 5 cm). Installation of the total system was completed until 1994 and dosimetry study (doserate and spectrum measurements) will be continued. We are now preparing proton beam extraction system for cell irradiation.

5 . Evaluation of ²⁵²Cf and monochromatic energy neutron and gamma ray absorbed doses and their beam qualities

Hoshi, M., Endo, S., Tanaka, K., Yoshikawa, I.^{*1}, Takatsuji, T.^{*1}, Fujikawa, K.^{*2}, Onizuka, Y.^{*3} and Uehara, S.^{*3} (^{*1}Nagasaki Univ., ^{*2}Kinki Univ., ^{*3}Kyushu Univ.)

A fission neutron source (half life 2.64 years) has a beam quality similar to the Hiroshima and Nagasaki A-bombs. This ²⁵²Cf source has been installed at RIRBM in 1984 to study biological effects of fission neutrons. A monochromatic neutron generator has been installed in RIRBM also. Evaluation of neutron and gamma ray absorbed doses in biological materials and beam qualities of them is the purpose of this study. For the evaluation of doses, paired chambers (a tissue equivalent chamber and a chamber which have sensitivity only to gamma rays) were mainly used, and absorbed dose rates of neutrons and gamma rays in air and in rat and mouse plastic phantoms were determined. To discuss beam qualities a Monte Carlo computer code is used to obtain calculated neutron spectra. This code is one of those used in the project of DS86 dose evaluation. Especially, iron materials (thicknesses are from 10 to 20 cm) are used as attenuator to modify the ²⁵²Cf neutron spectrum closer to that of Hiroshima DS86 neutrons. In this study, dosimetry of neutron beams will be performed, and beam quality in relation to RBE will be discussed. Actually, we are using Drosophila and Onion to study genetic effects and induction of micronuclei, respectively.

6 . Dosimetry study of neutrons from research reactor institute, Kyoto University and approaches to find their mechanism for biological materials

Hoshi, M., Endo, S., Tanaka, K., Onizuka, Y.¹, Uehara, S.¹, Kobayashi, T.², Sakurai, Y.², Takatsuji, T.³, Yoshikawa, I.³ and Utsumi, H.² (¹Kyushu Univ., ²Kyoto Univ., ³Nagasaki Univ.)

At the Research Reactor Institute, Kyoto University they are performing two studies such as (1) effects of radiation and (2) brain tumor therapy both using thermal and epi-thermal neutrons. In this study, we are measuring dose and quality of these neutrons. Based on these studies we perform the study to solve the mechanism of damages for biological materials in relation with the other high LET radiation such as HIRRAC mono_energetic neutrons at our institute. Also this study will correspond to the better control of brain tumor. For the evaluation of radiation doses we use three method of dosimetry such as activation of gold wire, LET counter measurements and paired chamber dosimetry and compare each other. For the evaluation of radiation quality, we use LET counter and ultra miniature counter (UMC). We consider relationship between effects of radiation with biological materials.

After this differences with HIRRAC neutrons will be compared. According to these studies we proceed the study of mechanism of the radiation effects for biological materials. Also we will consider the improvement of radiation therapy

technique from the side of accurate dosimetry.

7 . Study of contamination in environment and health effect of the residents in contaminated area according to the Chernobyl accident

Hoshi, M., Endo, S., Takada, J.¹¹, Tanaka, K., Orlov, M.², Takatsuji, T.³, Sato, H.⁴, Stepanenko, V. F.², Ivannikov, A. I.², Shinkarev, S.⁵ and Hayakawa, N.⁶ (¹Sapporo Medical University, ²MRRC RAMS, Russia, ³Nagasaki Univ., ⁴Ibaraki Pref. Univ. HIth. Sci., ⁵Biophys., Russia., ⁶Dept. Epidemiol.)

Examinations of the children in contaminated area according to the Chernobyl accident have been performed by the Chernobyl Sasakawa Medical and Health Cooperation Project (Chernobyl SMHC Project). The examinations begun in 1991 to help health care for the children of ages from 0 to 10 years old at the time of the accident and include three subjects concerning thyroid gland, blood and ¹³⁷Cs whole body counts. This study is to measure ¹³⁷Cs in the whole body and to calculate absorbed doses in them. The measurements of soil and food samples at each examiner's house are also planned and relation between children's body and soil contamination will be studied.

We have contracted between Medical Radiological Research Center Russian Academy of Medical Sciences in June 1998, and our institute continues collaboration concerning the problem of Chernobyl.

8 . Determination of A-bomb doses for survivors in Hiroshima

Hoshi, M., Endo, S., Tanaka, K., Ohtaki, M.¹ and Hayakawa, N.² (¹Dept. Environ. Biomet., ²Dept. Epidemiol.)

The radiation doses in Hiroshima and Nagasaki were determined for survivors who are registered at Radiation Effects Research Foundation (RERF). However, the estimation was limited in those at RERF. It was asked to construct a radiation dose estimation system for A-bomb survivors. This study was to make such system at RIRBM, Hiroshima University. It was discussed to make the system by using only published literatures. As a conclusion in such discussion, the best one was to use the Dosimetry System 1986 (DS86) which was published at RERF in 1987. A computer program to obtain estimated doses has been considered and the program was developed. The doses for the survivors calculated by this code are those at inside and outside of Japanese houses. For the estimation, most important factor is to determine distances from the hypocenter which should be known within 100m error. We will apply ABS93D for the rest of the registered survivors at RIRBM and will compared with those of RERF. The difference of typical dose was about 10%.

9 . Dosimetry study on Emergency health care

Hoshi, M., Endo, S., Tanaka, K. and Toyoda, S.^{*} (^{*}Okayama Univ. Science)

In the case of radiation accident, rapid dose evaluation for the exposed people is important for their health care. The effects of the radiation are totally different from the exposed dose levels. If the dose levels are very high, immediate care will be necessary. We have experiences of the radiation dosimetry in the cases of Semipalatinsk, Chernobyl, and Hiroshima and Nagasaki. However, these dosimetry studies have been performed long after the actual exposures. Therefore rapid dose-evaluation system is necessary to develop in the present program. There are mainly two types of radiations such as exposure by gamma rays and particles. The typical case of the latter one is neutrons. The neutron dosimetry is relatively not difficult since they induce many radioactivities, by which thermal and fast neutron doses will be evaluated. We will improve the methods of neutron dosimetry. However, for the gamma ray estimation, we have not so many ways. We can measure teeth enamel samples or perform dose reconstruction by calculation. In this study we will improve tooth enamel dosimetry and try to find any other way for the gamma-ray dose estimation.

- 372 -

10 . Gene-chemotherapy for gastrointestinal cancer patient

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The objective of this study is to assess a possibility of gene-chemotherapy by introducing bax gene into gastric cancer cells in combination with anticancer drugs. Using MKN45 gastric cancer cells, the bax cDNA deriving plasmid expression vector was injected with lipofectamine to the tumors transplanted into nude mice. The antitumor effect and induction of apoptosis was evaluated by NCI protocol and TUNEL method. We found that the overexpression of bax gene enhanced anticancer drugs such as 5-FU and CDDP in MKN45 gastric cancer in vivo. These results suggest that a potentiality of gene-chemotherapy by intratumoral injection of bax cDNA plasmid in gastric cancer.

11 . Analysis of molecular mechanism (s) of anticancer-induced apoptosis

Kim, R., Emi, M.¹, Tanabe, K.¹ and Toge, T.¹ (¹Dept. Surg. Oncol.)

The mechanism(s) by which anticancer drugs induced apoptotic cell death has been clarified in terms of caspase activation in mitochondria. One of the important events for the caspase activation is initiated by the induction of bax gene. We examined the involvement in activation of cysteine and serine proteases leading to apoptosis. The treatment with a pancaspase inhibitor blocked the sensitivity to ADM, SN-38 and CDDP in apoptosis. Further, the treatment with a caspase 3 inhibitor blocked the sensitivity to VP-16 and SN-38. Importantly, the treatment with a serine protease inhibitor, TLCK blocked the sensitivity to ADM, SN-38, CDDP and 5-FU, while the serine protease inhibitor, TPCK could not blocked any anticancer drugs tested. These results indicate that the caspase activation in down-stream event of apoptosis could be blocked in part by the cysteine and serine protease inhibitors in gastric cancer cells.

12 . Significance of apoptosis for overcoming drug-resistance in cancer chemotherapy

Kim, R., Emi, M.¹, Tanabe, K.¹ and Toge, T.¹ (¹Dept. Surg. Oncol.)

The resistance to apoptosis has been known as one of drug-resistance mechanism(s) in cancer chemotherapy. The overcoming drug-resistance by introducing an apoptosis-related gene, bcl-Xs was examined in human nasopharyngeal KB resistant cells. The enhancement of drug sensitivity was associated with the induction of apoptotic cell death without modulating intracellular drug concentration by a drug efflux pump MRP1. Of interest, the enhancement of dug sensitivity was completely reversed in the bcl-Xs-transfected cells by the treatment with BSO, that is an inhibitor of MRP1. Further, the enhancement of drug sensitivity in the bcl-Xs-transfected cells was superior than that of the treatment with BSO alone. These results suggest that intracellular drug concentration and signal transduction of apoptosis-related gene were independent factor in apoptosis in the modulation of drug sensitivity in resistant cells, and that both factors are essential for determining drug-sensitivity in cancer cells.

13. Significance of receptor-dependent signaling pathway in anticancer drug-induced apoptosis

Kim, R., Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The pathways of anticancer drug-induced apoptosis have been reported in receptor-dependent and -independent signal transductions. The receptor-dependent pathway is mediated by the activation of Bax, that is connected to the release of cytochrome c and the activation of caspase 3 leading to apoptosis. In contrast, the receptor-independent pathway is mediated by Fas and DR4 or DR5. The significance of the receptor-independent pathway is not unclear. To assess the clinical significance of the receptor-dependent pathway, we investigated the expression of Fas, DR4 and DR5 following the treatment with anticancer drugs in MDA-MD-231 breast cancer cells. The expression of DR4, DR5 and Fas was predominantly induced by the treatment with MMC, ADM and TAX, respectively. These induction of the receptor signaling

pathways were associated with the activation of caspase-8, release of cytochrome c and the activation of caspase-3 in apoptosis. The modulation of the receptor signaling pathways for enhancement of drug sensitivity is under investigation. The increase in expression of DR4, DR5 and Fas is different from each drugs tested. These results suggest that anticancer drug-induced apoptosis is mediated by different death receptor, which is connected to activation of caspase-8 leading to apoptosis.

14. Overcoming of drug-resistance by down-regulation of Bcl-2 using antisense Bcl-2

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The objective of this study is to an attempt in overcoming of drug-resistance due to the overexpression of Bcl-2 using antisense bcl-2. The introduction of antisense bcl-2 enhanced the drug sensitivity to MMC and TAX in MDA-MB-231 breast cancer cells. The enhancement of drug sensitivity was associated with the induction of apoptosis. Further, drug-resistance also associated in part with overexpression of bcl-2 in breast cancer cell lines. The relationship between overexpression of bcl-2 and other drug-resistance factors is under investigation. The final goal would be to determine which factor is most important for the modulation of drug sensitivity in resistant cells. The introduction of antisense Bcl-2 in MDA-MB-231 cells enhanced the sensitivity to MMC and paclitaxel associated the activation of Fas, caspase-8, cytochrome c leading to apoptosis.

15 . Enhancement of drug-sensitivity by antisense HER-2 in breast cancer cells

Kim, R., Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The overexpression of HER-2 was involved in drug-resistance in breast cancer cells. The down-regulation of HER-2 by anti-HER-2 antibody increased drug-sensitivity such as ADM and Taxanes. We investigated whether the down regulation of HER-2 by antisense HER-2 increased drug-sensitivity in breast cancer cell lines. The treatment with antisense HER-2 increased the sensitivity to TAX in BT-474 breast cancer cells. The down-regulation of HER-2 was associated in part with the decrease of Bcl-2. The influence to other drug-resistance factor such as P-gp and MRP1 in the antisense HER-2-treated cells is under investigation. The mechanisms(s) by which antisense HER-2 increased drug sensitivity will be clarified in terms of the signal transduction pathways in apoptosis. The treatment with antisense HER-2 in BT-474 breast cancer cells enhanced the drug-sensitivity to MMC, ADM, TXT, and TXL associated with apoptosis. The induction of apoptosis is correlated with activation of Bax, Fas, casapase-8, cytochrome c and caspase-3 leading to apoptosis.

16 . Enhancement of drug-sensitivity by antisense Bcl-2 in gastric and breast cancer cells

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The overexpression of HER-2 was involved in drug-resistance in gastric cancer cells. We investigated whether the down regulation of HER-2 by antisense HER-2 increased drug-sensitivity in gastric cancer cell lines. The treatment with antisense HER-2 increased the sensitivity to CDDP in MKN45 gastric cancer cells. The down-regulation of HER-2 was associated in part with the decrease of Bcl-2. The mechanisms(s) by which antisense HER-2 increased drug sensitivity will be clarified in terms of the signal transduction pathways in apoptosis. The treatment with antisense HER-2 in MKN45 gastric cancer cells enhanced the drug-sensitivity to CDDP associated with apoptosis. The induction of apoptosis is correlated with activation of Bax, Fas, casapase-8, cytochrome c and caspase-3 leading to apoptosis. In a similar fashion, antisense Bcl-2 enhanced chemotherapeutic effect of anthracyclines and taxanes in BT-474 and ZR-75-1 breast cancer cells.

17. Enhancement of therapeutic effect in combination treatment with imatinib and anticancer drug in gastric and breast carcinoma

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

[Background and Objective] Imatinib (STI571, Gleevec) is a novel molecular targeting agent, which inhibits the activity of c-kit and PDGFR in gastrointestinal stromal tumors, as well as to inhibit the tyrosine kinase activity of Bcr-Abl in CML and ALL. We conducted preclinical evaluation of therapeutic effect of imatinib and potential synergism in combination with imatinib and anticancer drug in gastric carcinoma cells, in terms of growth inhibition by targeting PDGF/PDGFR signaling pathway. [Materials and Methods] MKN-45 gastric carcinoma cells were employed, and the cells were transplanted into nude mice. When the tumor size was reached approximately 100 mm after transplantation, the mice were arbitrarily divided in four groups (n=8/group), according to no treatment, treatment with anticancer drug alone, treatment with imatinib alone, and combination treatment with imatinib and anticancer drug, respectively. Imatinib was administered intraperitoneally at 50 mg/kg for consecutive 28 days, whereas anticancer drug was administered at LD₅₀/3 four times in gwk. Antitumor effect was evaluated by NCI protocol. Apoptosis and gene expression was assessed by TUNEL assay, Western blotting, and immunohistochemical staining, respectively. [Results and Discussion] The treatment with imatinib of MKN-45 gastric carcinoma xenograft showed antitumor effect to a greater extent than the treatment with 5-fluorouracil (5-FU) or docetaxel (TXT) alone. Further, antitumor effect was significantly enhanced in the combination treatment with imatinib and 5-FU or TXT, compared to the treatment with imatinib, 5-FU or TXT alone (P<0. 01, Student t-test). Decrease in the body weight loss in the mice cotreated with imatinib and 5-FU or TXT was less than 10 %. Enhanced antitumor effect in combination treatment with imatinib and anticancer drug was associated with both induction of apoptosis and inhibition of tumor angiogenesis, which was explained with the decreased expression in pAkt, and PDGF-betaR, and decreased phosphorylation of PDGF-betaR. In the way of similar mechanism, combination treatment with STI571 enhanced the chemotherapeutic effect of TXL and TXT. These results suggest that combination treatment with imatinib and anticancer drugs such as 5-FU and TXT may a new strategy for enhancing therapeutic effect in the treatment gastric carcinoma, due to targeting inhibition of PDGFR-mediated paracrine tumor growth.

18 . Rationale for endocrine-chemotherapy in breast cancer

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The therapeutic efficacy of endocrine-chemotherapy has been revealed in receptor positive and node positive breast cancer patients. However, the survival benefit of endocrine-chemotherapy in these patients seems too small compared to receptor negative patients with node positive. Based on these findings, we are planning to investigate whether the treatment with TAM can decrease the therapeutic effect of anticancer drugs in receptor positive patients with breast cancer. Using in vitro model, the effect of introduction of bcl-2 gene into breast cancer cells will be assessed. Further, whether the treatment with TAM can induce the expression of Bcl-2 associated with drug resistance will also be tested. From these findings, the optimal schedule for endocrine-chemotherapy will be evaluated for adjuvant setting in receptor positive and node positive patients with breast cancer. Treatment with Estradiol in MCF-7 increased expression of Bcl-2, resulted in the decrease of sensitivity to anticancer drugs.

19. Clinical significance of a new drug-transporter gene, BCRP in breast cancer

Kim, R., Uchida, Y.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The objective of this study to assess clinical significance of the drug-transporter gene, BCRP in breast cancer patients. Using in vitro model, the relationship between the expression of BCRP gene and drug sensitivity will be tested, and the effect of introduction of BCRP gene into breast cancer cells with its low expression will also be examined. Further, the

protein expression of BCRP will be assessed in the drug-resistant patients with the failure in prior chemotherapy. Of interest, the other drug-resistance factors including BcI-2, HER-2 and other membrane transporter proteins will be investigated in the transfected cells. The clinical significance of BCRP gene will be evaluated in the clinical situation. The expression of BCRP is closely correlated with the sensitivity to ADM, and overexpression of BCRP is associated with in part resistance to 5-FU. The sensitivity to MMC and TXL is involved in other factors contributing to drug-sensitivity in breast cancer cells. The expression of BCRP is dominantly related with sensitivity to ADM, and the overexpression of BCRP may cause the resistance to 5-FU in breast cancer cells.

20. Studies on sentinel lymph node biopsy and micrometastasis in breast cancer patient

Kim, R., Osaki, A.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The objectives of this study to establish the standard procedure of sentinel lymph node biopsy (SLNB) in node negative breast cancer for elimination of axillar lymph node dissection (ALND), and to assess the clinical significance of micrometastasis in SLNs. Using Tc-99m human serum albumin (HSA) and tin colloid in 23 breast cancer patients, the overall predictive rate and false negative rate were 85.7% and 14.2%, respectively. The direction of SLN was observed to internal mammary side in about 20%, and the micrometastasis assessed by RT-PCR for CEA, CK19 and MUC1 was found in one case of 8 patients with node negative. The all patients underwent backup ALND after the SLNB. The clinical usefulness of Tc-99m phytate is being under investigation. The overall predictive rate over than 85.0% and false negative rate less than 10% will be allowed to spare ALND. The clinical significance of micrometastasis will be assessed in the survival. The micrometastasis is rare in node negative lymph nodes, suggesting that the micrometastasis in node negative lymph node may not be involved in a prognostic factor in breast cancer patients.

21. Clinical significance of micrometastasis of bone marrow in breast cancer patient

Kim, R., Osaki, A.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The poor prognosis with the presence of micrometastasis in bone marrow has been known in previous studies. We are planning to investigate the clinical significance of internal mammary node in bone marrow micrometastasis in terms of the survival, since it is not unclear whether the drainage lymph node with cancer cells can cause bone marrow metastasis. Especially, the relationship between internal mammary direction of SLN and bone marrow micrometastasis will be assessed. Further, an additional adjuvant chemotherapy for the micrometastasis in bone marrow will be designed to assess the survival benefit. The micometastasis in bone marrow is seen in a node-negative patients, suggesting that micometastasis in bone marrow is observed in node-negative breast cancer patients, suggesting that the micrometastasis may be an independent prognostic factor to influence the survival.

22 . Gene therapy by antisense Bcl-2 and HER-2 in undifferentiated thyroid cancer

Kim, R., Emi, M.^{*1}, Tanabe, K.^{*1} and Toge, T.^{*1} (^{*1}Dept. Surg. Oncol.)

The objective of this study to assess the enhancement of drug sensitivity by introducing antisenseBcl-2 or HER-2 into the 8503 C undifferentiated thyroid cancer cells. The therapeutic efficacy of chemo-radiation in patients with undifferentiated thyroid cancer is limited. We are planning to investigate the effect of introduction of bax gene in undifferentiated thyroid cancer cells, since antisense Bcl-2 and HER-2 have a key role in expressing apoptotic cell death in combination with anticancer drugs. The final goal would be the improvement of survival in patients with undifferentiated thyroid cancer. The new approach in the strategy to enhance antitumor effect will be tested. The treatment with antisenseBcl-2 or HER-2 enhanced drug-sensitivity including ADM, MMC, CDDP, 5-FU, TXL, and TXT associated with apoptosis. The

mechanisms by which antisense BcI-2 or HER-2 enhanced drug-sensitivity are explained by activation of Fas, caspase-8, cytochrome c and caspase-3 leading to apoptosis.

23. Research for the secondary fragments from the therapeutic carbon beam at HIMAC

Endo, S., Tanaka, K., Hoshi, M., Onizuka, Y.^{*1}, Takada, M.^{*2}, Fukumura, A.^{*2}, Hayabuchi, N.^{*3}, Ishikawa, M.^{*4} and Maeda, N.^{*5} (^{*1}Kyushu Univ., ^{*2}NIRS, ^{*3}Kurume Univ., ^{*4}Univ. of Tokyo, ^{*5}Izumisano Hospital)

Purpose of this study is evaluation of the therapeutic heavy ion field at HIMAC, NIRS using the microdosimetry technique. At the results of the previous experiments, Onizuka et al. showed that the relative biological effectiveness (RBE) at the deeper part in tissue was not very strong. These trends differ from the data of LET-RBE relations, which is used for the basic data of therapeutic irradiation. We want to understand how come the differences. To do this, we measure the microdosimetric spectrum for carbon beam and the secondary fragments particles, separately. The microdosimetric spectrum for each fragment and RBE are discussed precisely.

24 . Evaluation of the neutron and gamma-ray mixed field at UTR-KINKI

Endo, S., Tanaka, K., Hoshi, M., Fujikawa, K., Horiguchi, T. and Ito, T. (Kinki Univ.)

Neutron energy spectra measurements of UTR-KINKI using the foil activation method coupled with artificial neural network were performed in 1999-2001. From this study showed characteristics of the neutron field at UTR-KINKI. On the other hand, Fujikawa et al. who is collaborator of this study has shown the biological effectiveness of neutron. In this study, microdosimetric evaluation using LET-counter as the next step. The microdosimetric technique can analyze the relative biological effectiveness from measured spectrum.

25 . Development of Imaging PIXE

Endo, S., Tanaka, K., Hoshi, M. and Shizuma, K.^{*} (^{*}Grad. Sch. Eng.)

It can contribute to the new research and the development in the field of the medical and material sciences that can analyze the 2 dimensional profile of the element formation. A trace element using the PIXE analysis method which the ion beam from the MeV-accelerator is established for recent thirty years. As 2 dimensional element mapping, a micro-beam was used with PIXE have been tested recently. The structure that the vibration of the beam line is restrained, and enough length are necessary, and a micro-beam costs about one billion yen. On the other hand, SPECTdeveloped recently and used in the medical diagnosis (Single Photon Emission Computer Tomography). If we succeed that the PIXE is combined with the SPECT technique, the 2 dimensional element mapping at the usual accelerator facilities without a micro-beam line can be available.

26 . Research for the initial interaction of neutron with biological materials

Endo, S., Tanaka, K. and Hoshi, M.

For many years at Hiroshima University, we have studied the radiobiological effects of atomic-bomb neutrons using a neutron generator (HIRRAC). Recent developments in track-structure studies and biophysical modeling have made it possible to make an attempt to simulate tracks of low energy neutrons at a molecular level using Monte Carlo track structure simulation methods. In general, neutron collisions with atomic nuclei lead to recoil atomic ions and nuclear reaction products in the form of secondary charged particles. The energies of these particles vary according to the energy of the incident neutrons. In hydrogen containing media such as water and tissue the most important interaction is elastic scattering with hydrogen nuclei (protons), which accounts for more than 90% of energy transfer. Protons are, therefore,

- 376 -

considered to be the most important recoil particles for estimating neutron induced radiation effect. The recoil protons and other ions set in motion in the cell, in turn, interact with the bio-molecule leading to DNA damage and subsequent biological lesions. Most of these recoil protons are low energy particles below 1 MeV energy. Therefore, the motivation for this work arises for a need to simulate the tracks of low energy protons emitted in neutron interactions in tissue as these simulations are needed in biophysical modeling. Although proton track simulation at energies above the Bragg peak has been achieved to a high degree of precision simulations at energies near or below the Bragg peak have not been attempted because of the lack of relevant cross section data. As the hydrogen atom has a different ionization cross section from that of the proton, charge exchange processes (CEP) need to be considered in order to calculate the electronic stopping power for low energy protons. In this study, we have used state of the art Monte Carlo track simulation techniques, in conjunction with the published experimental and established theoretical data, to develop a model for the extension of the proton track simulation in the low energy region.

27 . Research for the initial interaction of neutron with biological materials

Endo, S., Tanaka, K., Hoshi, M., Nagashima, Y.^{*1}, Sasa, K.^{*1}, Yamamoto, M.^{*2} (^{*1}University of Tsukuba, ^{*2}Kanazawa University)

The nuclear test of 467 times in total was done at Semipalatinsk nuclear test site of the old Soviet Union between 1990's from 1949. It made 19Mt in total when output is converted into the TNT gunpowder. Radioactivity diffused into the atmosphere, and influenced the large area of about 500km by radioactive fallout. The radioactive fallout was cause of external and internal exposure. The international collaboration was continued to investigate the dose evaluation and health care for the *hibakusha* from 1993 to 2005. Recently, inspection by the supersonic medical examination device of the thyroid gland are done, and it was found disease in high frequency. The disease of such a thyroid gland can be thought the influence of radioactive iodine I-131 from a fission product. Furthermore, it has already been clear by Chernobyl accident investigation that the internal exposure from I-131 is dominant. However, there are no data of the radioactive I-131, because it can't be measured any more after the day when a nuclear test was done at several weeks due to the short life of I-131 (eight days). Soil samples are collected from the circumference of Semipalatinsk nuclear test area. If a released long life (1.57 × 10⁷ years) I-129 at the same time can be measured, we might determine the effects of I-131. Because a chemical property of I-131 and I-129 is the same, and it becomes possible that it guesses the polluted conditions of I-131.

28 . Characterization of the two murine mutants, Pax6^{Sey3H} and Pax6^{Sey4H}, which delete the region of a putative tumor suppressor gene of acute myeloid leukemia on chromosome 2

Nitta, Y. and Yoshida, K.^{*1} (^{*1}Natl. Inst. Radiol. Sci.)

Radiation-induced acute myeloid leukemias (AML) in the mouse are characterized by chromosome 2 deletions. We found that a DNA segment, D(2)Mit15 has been deleted in 92.5% of AMLs by FISH (2002). To perform positional cloning of an tumor suppressor gene near the D(2)Mit15 region, two mutant strains of mice, Pax6^{Sey3H} and Pax6^{Sey4H}, which exhibit hemizygous deletion of the Pax6 region on chromosome 2. The radiation-induced, chemical-induced and spontaneous tumoriginicity of these mutants have been characterized. Myeloid leukemia was induced by radiations with shorter latency. Female was more susceptible to radiation myeloid genesis than male (2004).

29. Internal exposure to Radioactive Iodine (I-131) and thyroid carcinogenesis

Nitta, Y., Watanabe, R¹. and Akimoto, Y.² (¹Japan Atomic Energy Organization, ²Div. Genome Response)

Short latency for the development of thyroid cancer in the post-Chernobyl cases proposes us to make sure the thyroid susceptibility to internal exposure at young ages. We have established an experimental model of internal exposure to I-131

in rats. Standard curves for the estimation of their absorbed fraction of the gamma-ray in the thyroid have been proposed for1-, 4- and 9-week-old rats (1998). Then, standard curves for the estimation of their absorbed doses have been shown for the three age groups (2001). Radiation susceptibility of the thyroid to I-131 has been compared by the histopathological appearance, apoptosis and proliferation profiles of the thyroid epithelium among the three age-groups (2001, 2002). Carcinogenicity of internal vs external radiation has been compared in the rat thyroid carcinogenesis model (2004).

30 . Research on the biological effects of neutron at low energy levels (~1.0MeV)

Nitta, Y. and Araki, N.^{*1} (^{*1}Kagawa Univ.)

Purpose: To investigate the direct and delayed biological effectiveness of neutrons on the mouse ovarian apoptosis and carcinogenesis, and mouse inner ear toxicity.

Materials and methods: Female mice were exposed to 1.0Gy of monoenergetic neutrons (1.03MeV), ²⁵²Cf fission neutron (2.13MeV) or ¹³⁷Cs -rays at 7 days of age. The kinetics of oocyte apoptosis was studied. Ovarian carcinogenesis was observed pathologically. Granulosa cell tumor development was tested in 3.0Gy ⁶⁰Co -irradiated ovaries, which were transplanted into non-irradiated recipients.

Results: Tubular adenomas developed in the neutron- and -irradiated mice, whereas, granulosa cell tumors developed only in -irradiated mice. The direct effect to induce oocyte apoptosis was quantitatively stronger at high than low LET-radiation. The delayed effectiveness on ovarian carcinogenesis was reciprocal. The origin of tubular adenomas and granulosa cell tumors could be the pregranulosa cells of the primary follicles, whose oocytes were dead in the former and alive in the latter. To confirm the qualitative difference of radiations between high-LET and low-LET, radiations susceptibility of inner ear has been examined. Neutrons induced acute and subclonic changes in the inner ear (2005).

31. Development a supporting system of elderly residents in a local community

Nitta, Y., Harada, T.⁻¹, Ishizaki, F.⁻², Nitta, K.⁻³ and Ootani, H. (⁻¹Hiroshima International Gakuin Univ., ⁻²Hiroshima Prefecture College of Health Science, ⁻³Ootani Rehabilitation Hospital),

The purpose is to clarify the relationship of physical, sociological and psychological factors to health status in community elderly residents, and then to develop a supporting system of elderly residents with the help of companion animals. Subjects were 100 elderly residents aged 60-90 years living at home in Oogaki, a rural town of Hiroshima prefecture. A baseline comprehensive health survey was performed by Medical doctors. The interview of activities of daily living (ADL) has been performed once per year (2003). An analysis of apolipoprotein E polymorphism in ages patients with vascular dementia (2004).

32 . Database of Testimones by hibakusha

Kawano, N., Hirabayashi, K., Hoshi, M., Matsuo, M.¹, Satoh, K.² and Ohtaki, M.² (¹Institute for Peace Science, ²Dept. Environ. Biomet.)

We attempt at making database of testimonies by *hibakusha*. These *hibakusha*'s testimoneis are collected by International Radiation Information Center and Institute for Peace Science, Hiroshima University. We continue to input full text of testimonies into a computer. Now we can retrieve any words in the testimonies. We will try to open the database to the public, but we consider the issues of *hibakusha*'s privacy and the copyright on a book. This is a joint research project with Dept. Environ. Biomet of RIRBM and Institute for Peace Science, Hiroshima University.

- 378 -

33 . Content Analysis of Testimonies by hibakusha

Kawano, N., Hirabayashi, K., Hoshi, M., Satoh, K.⁻¹, Ohtaki, M.⁻¹ and Matsuo, M.⁻² (⁻¹Dept. Environ. Biomet., ⁻²Institute for Peace Science)

We attempt to clarify the realities of atomic bomb dropped on Hiroshima in 1945. For this purpose, we analyze the content of witnesses of *hibakusha*. First, we try to answer a question, "who wrote the witnesses of *hibakusha* and what were they watching and writing?" Second, we choose the words or terms in the witnesses of *hibakusha* which are often used. We clarify the realities of atomic bomb in terms of analyzing the terms or words. We will continue this research for a long time.

34 . Research on the realities of hibakusha in Semipalatinsk, Kazakhstan

Kawano, N., Hirabayashi, K., Taooka, Y., Hoshi, M., Hiraoka, T. and Ohtaki, M.' ('Dept. Environ. Biomet.)

We use questionnaires to clarify the realities of *hibakusha* in Semipalatinsk. The questionnaires will be based on previous investigations carried out by the former Ministry of Health and Welfare, Hiroshima city, Nagasaki city, and Japan Confederation of A- and H- Bomb Sufferers Organizations. We also attempt to collect the testimonies of *hibakusha* in Semipalatinsk. We will analyze the content of testimonies to clarify their realities. Then, we try to explore the realities of *hibakusha* in Semipalatinsk in terms of the questionnaires and the witnesses. It is possible to clarify their life environment and health condition by means of the questionnaires. The testimonies will show their suffering. Finally, we compare the realities of *hibakusha* in Semipalatinsk with those in Hiroshima and Nagasaki. By this comparison, radiation effects on *hibakusha* will be more clear.

In 2004, we collected 283 respondents and 237 testimonies from *hibakusha* in Semipalatinsk. We continue this research project.

35. Database of the materials concerning the Hiroshima and Nagasaki atomic bombings and other radiation exposures

Kawano, N., Hoshi, M., Hiroshima University Library, Kamiya, K.¹¹ (¹¹Dept. Exp. Oncol.)

We are now making the database of the materials concerning the Hiroshima and Nagasaki atomic bombings and other radiation exposures. This research project is supported by Grant-in-Aid for Publication of Scientific Research Results. We input the following data into the computer:

- 1. Newspaper articles concerning the Hiroshima and Nagasaki atomic bombings and other radiation exposures.
- 2. The materials related to A-bombs returned by the AFIP in the U.S.
- 3 . Books concerning the Hiroshima and Nagasaki atomic bombings and other radiation exposures.
- 4. Data of physical materials concerning the Hiroshima and Nagasaki atomic bombings.
- 5 . Data of US nuclear tests and the former USSR nuclear tests.
- 36 . Accelerator-based neutron irradiation system for Boron Neutron Capture therapy

Tanaka, K., Endo, S., Hoshi, M., Kobayashi, T.^{*1}, Bengua, G.^{*1} and Nakagawa, Y.^{*2} (^{*1}Kyoto University, ^{*2}National Kagawa Children's Hospital)

Boron Neutron Capture Therapy (BNCT) is appreciated for its high "Quality of Life (QOL)" derived from the possibility to destroy tumor cells selectively in cellar lever in principle. So far, BNCT treatments has been conducted using reactors. In this case, patients have to move to irradiation facilities, which are far from hospitals, after surgery to debulk the tumor. Installation of the accelerators for BNCT at hospitals will reduce patients' load and risk due to transport. The accelerator-based neutron irradiation systems for BNCT are studied in this topic. The use of ⁷Li(p,n)⁷Be neutrons at near-threshold

energies and those by 2.5 MeV protons are assumed at present.

37. Evaluation of dose by the ¹⁰B (n,)⁷Li reaction in Boron Neutron Capture Therapy

Tanaka, K., Endo, S., Hoshi, M., Kobayashi, T.^{*1}, Bengua, G.^{*1} and Nakagawa, Y.^{*2} (^{*1}Kyoto University, ^{*2}National Kagawa Children's Hospital)

The advantage of BNCT is the possibility to destroy tumor cells selectively in cellar lever in principle. This would be realized by concentrating ¹⁰B(n,)⁷Li dose into tumor cells. The final goal of this study is 3-dimensional and on-time evaluation of ¹⁰B(n,)⁷Li dose in *in-vivo* medium. As its first step, the usage of imaging plates will be investigated for 2-dimensional evaluation of ¹⁰B(n,)⁷Li reaction distributions.

38 . Genetic pathway in molecular pathogenesis of myelodysplastic syndrome (MDS) with AML1 point mutations

Harada, Y., Harada, H.⁻¹, Ding, Y.⁻¹, Imagawa, J.⁻², Niimi, H.⁻¹, Kyo, T.⁻³, Inaba, T.⁻⁴, Kimura, A.⁻¹ (⁻¹Dept. Hematol. Oncol., ⁻²Ohtake National Hospital, ⁻³Hiroshima Red Cross Hospital and Atomic-bomb Survivors Hospital, ⁻⁴Dept. Mol. Oncol.)

AML1 mutations have been reported to be frequent in myelodysplastic syndrome (MDS) patients, especially those with refractory anemia with excess blast (RAEB), RAEB in transformation (RAEBt), and AML following MDS (defined these categories as MDS/AML). Although AML1 mutations are suspected to play a pivotal role for developing MDS/AML, acquisition of additional genetic alterations is necessary. We analyzed gene alterations in patients with AML1 mutations, comparing with those without AML1 mutation, and detected specific gene alterations in AML1-mutated MDS/AML patients. Now we are inducing both mutants of these genes and AML1 mutation thematopoietic stem cells, and analyzing biological changes of these cells. Furthermore, we are going to inject these cells into mice and check development of MDS. Using this approach, we are able to clarify the molecular pathogenesis of MDS.

39. Myelodysplastic syndrome (MDS) among atomic-bomb survivors and radiation-exposed residents near the Semipalatinsk nuclear test site

Harada, Y., Harada, H.⁻¹, Zharlyganova, D., Ding, Y.⁻¹, Kyo, T.⁻², Hoshi, M., Kimura, A.⁻¹ (⁻¹Dept. Hematol. Oncol., ⁻² Hiroshima Red Cross Hospital and Atomic-bomb Survivors Hospital)

Increased risk of myelodysplastic syndrome (MDS) has been shown in atomic-bomb survivors. We showed that AML1 point mutations were found in half of MDS patients among atomic-bomb survivors in Hiroshima. To clarify the molecular mechanism of radiation-induced MDS, we are performing mutation analysis of genes including transcriptional factors and tumor suppressors in the patients with MDS in atomic bomb survivors and radiation-exposed residents near the Semipalatinsk nuclear test site.

40 . Molecular mechanism of secondary myelodysplastic syndrome (MDS) / acute leukemia (AML)

Harada, Y., Harada, H.¹, Ding, Y.¹, Niimi, H.¹, Kimura, A.¹ (¹Dept. Hematol. Oncol.)

Secondary MDS or AML arise after chemotherapy or radiation exposure for other malignancies. We and others have shown that high frequency of AML1 point mutation or AML1-related translocation was observed in patients with secondary MDS or AML. To clarify the molecular mechanism of secondary MDS or AML, we are trying to detect AML1 gene alteration induced by radiation or anti-cancer drug in human hematopoietic stem cells purified from cord blood cells.

- 380 -

I. Original papers

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- 386 -

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- 388 -

Symposium "International intercomparison of radiation dose estimation near Semipalatinsk nuclear test site - For the dose estimation in Dolon village - ", Hiroshima, March 9-11, 2005. (R, I)

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- 390 -

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- 70. Kawano, N.: Human suffering effects of nuclear tests at Semipalatinsk: an analysis of testimonies, Peace studies association of Japan, Sapporo, June 25, 2004
- 71. Kawano, N.: Effects of radiation exposure on the residents at the Semipalatinsk Nuclear Test Sites, Kazakhstan. The Peace Studies Association of Japan, Tokyo, Nov. 6, 2004.
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("Institute for Environmental Sciences, "²Takeichi Clinic, "³Kazakh Research Institute for Radiation Medicine and Ecology, Kazaskhstan) : Unstable type chromosome aberrations in lymphocytes from individuals living near Semipalatinsk nuclear test site. 3rd Dosimetry Workshop on the Semipalatinsk Nuclear Test Site Area with 10th Hiroshima International Symposium "International intercomparison of radiation dose estimation near Semipalatinsk nuclear test site - For the dose estimation in Dolon village - ", Hiroshima, March 9-11, 2005. (R, I)

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III. Others

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- Hoshi, M.: Physical Effects of Atomic Bomb Radiation. Hiroshima Nagasaki Seminar. Hiroshima, June 29, 2004. (R, I)

- 394 -

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- 5 . Hoshi, M.: Dosimetry study of Hiroshima and Nagasaki, and Semipalatinsk. A Meeting for the Chernobyl investigation team and medical examination. Hiroshima, February 20, 2005. (R, I)
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- 396 -