## Program at a Glance

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Program

July 31, 2009 (Fri)

18:30-20:30  Welcome Reception  (Hotel New Castle)

August 1, 2009 (Sat)

9:00-  Registration

9:30-9:35  Opening & Welcome  
Prof. Masahiko Endo, President of Hirosaki University

9:35-10:20  Symposium I  
Chair: Prof. Takashi Kondo, Toyama University, Japan

9:35-9:50  Effects of mesenchymal stem cell transplantation in preventing radiation-induced intestinal injury in mice
K. Kudo 1, Y. Liu 2, K. Takahashi 1, K. Tarusawa 1, D.-L. Hu 3, I. Kashiwakura 1, H. Kijima 4, and A. Nakane 3
1 Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences, Japan.
2 Particle Radiation Oncology Research Center, Research Reactor Institute, Kyoto University, Japan.
3 Department of Microbiology and Immunology, Hirosaki University Graduate School of Medicine, Japan.
4 Department of Pathology and Bioscience, Hirosaki University Graduate School of Medicine, Japan.

9:50-10:05  Recovery of the hematopoietic system after murine allogeneic umbilical cord blood transplantation
H. Sato, K. Ito, and K. Ito
Department of Biomedical Sciences, Hirosaki University Graduate School of Health Sciences, Japan.

10:05-10:20  Correlations of cell surface antigens with the individual differences of radio-sensitivity in human hematopoietic stem/progenitor cells
S. Monzen, N. Hayashi, K. Takahashi, and I. Kashiwakura
Department of Radiological Life Sciences, Hirosaki University Graduate School of Health Sciences, Japan.

10:20-11:05  Symposium II  
Chair: Dr. Yoichi Oghiso, Institute for Environmental Sciences, Japan

10:20-10:35  Radiation Emergency Medical Preparedness in Japan and a Criticality Accident at Tokai-mura
M. Akashi
Research Center for Radiation Emergency Medicine, National Institute of Radiological Sciences (NIRS), Japan
10:35-10:50 Overview of NIRS Educational Programs on Radiation Emergency Medical Preparedness
H. Tatsuzaki
Diagnosis Section, Department of Radiation Emergency Medicine, Research Center for Radiation Emergency Medicine, National Institute of Radiological Sciences (NIRS), Japan

10:50-11:05 Chromosome abnormality as a genetic indicator for radiation dose assessment and carcinogenesis
M. A. Yoshida
Biodosimetry Section, Department of Radiation Dose Assessment, Research Center for Radiation Emergency Medicine, National Institute of Radiological Sciences (NIRS), Japan.

11:05-11:20 Break

11:20-11:50 Symposium III
Chair: Prof. Mikinori Kuwabara, Hokkaido University, Japan

11:20-11:35 Experimental Studies on Biological Effects of Continuous Exposure of Mice to Low-Dose-Rate Gamma-Rays in a Special Reference to Transgenerational Effects and Biological Defense System
Y. Oghiso
Department of Radiobiology, Institute for Environmental Sciences, Japan

11:35-11:50 Chromosome Aberration Rates in Spleenocytes and Genomic Alterations in Malignant Lymphoma from Mice Long-Term Exposed to Low-Dose-Rate Gamma-Rays
K. Tanaka
Department of Radiobiology, Institute for Environmental Sciences (IES), Japan

11:50-13:00 Lunch

13:00-13:45 Symposium IV
Chair: Dr. Kiyomitsu Kawachi, Nuclear Safety Technology Center, Japan

13:00-13:15 Radiation Detection and Measurement in Patients Contaminated with Alpha Emitters
T. Momose, O. Kurihara, C. Takada, and S. Furuta
Radiation Protection Department, Nuclear Fuel Cycle Engineering Laboratories, Japan Atomic Energy Agency, Japan.

T. Miyakawa, and Y. Jin
Japan Nuclear Fuel Ltd, Japan.

13:30-13:45 DTPA Administration Methods for Accidents of α Particle Contamination
Y. Jin
Emergency Medicine Team, Japan Nuclear Fuel Ltd, Japan.
13:45-14:35  **Symposium V**  
Chair: Dr. Yutaka Jin, Japan Nuclear Fuel Ltd, Japan

13:45-14:35  **Shandong Radiation Exposure October 21, 2004**  
Y. Jin¹, and X. Chen²  
¹ Emergency team, Japan Nuclear Fuel Ltd., Japan  
² Beijing Institute of Radiation Medicine, China

14:35-14:45  **Break**

14:45-16:25  **Symposium VI**  
Chair: Dr. Makoto Akashi, NIRS, Japan

14:45-15:35  **A New Therapeutic Approach for Radiation Burns combining Surgery and Mesenchymal Stem Cell Administrations: About four cases**  
E. Bey¹ and J. J. Lataillade²  
¹ Hôpital d’Instruction des Armées Percy, Service de Chirurgie Plastique, Avenue Henri Barbusse, 92141 Clamart, France.  
² Hôpital d’Instruction des Armées Percy, Centre de Transfusion Sanguine des Armées Jean Julliard, Département Recherches et Thérapies Cellulaires, BP 410, 92141 Clamart, France.

15:35-16:25  **Mesenchymal Stem Cells as Drug Cells for Radiation Burn Treatment**  
E. Bey¹ and J. J. Lataillade²  
¹ Hôpital d’Instruction des Armées Percy, Service de Chirurgie Plastique, Avenue Henri Barbusse, 92141 Clamart, France.  
² Hôpital d’Instruction des Armées Percy, Centre de Transfusion Sanguine des Armées Jean Julliard, Département Recherches et Thérapies Cellulaires, BP 410, 92141 Clamart, France.

16:25-16:30  **Closing Remarks**  
Prof. Hitoshi Tsushima, Head of Hirosaki University Graduate School of Health Sciences

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**Instruction for Speakers**

**Presentation**  
The symposiums of The 1st International Symposium on Radiation Emergency Medicine in Hirosaki University consist of invited talks as well as contributed orals. Foreign Invited talks are allocated 45 minutes for presentation plus 5 minute for discussion. Domestic Invited talks and Regular Oral presentations will be 10 minutes long followed by a 5-minutes discussion.

A windows-based PC will be provided in the conference room. We strongly encourage you to use this computer facility. In this case please bring with you the presentation as PowerPoint or Pdf on CD or USB stick. If you prefer to use your own PC for your presentation, please inform operation staff in advice.

**Proceedings**  
The proceedings of The 1st International Symposium on Radiation Emergency Medicine in Hirosaki University will be published from Hirosaki University Press.
Flour Plan

1F
- Office of Communication Center
- Entrance
- Registration

2F
- Conference Room
- down to 1F
- up to 2F
Abstract
Effects of mesenchymal stem cell transplantation in preventing radiation-induced intestinal injury in mice

Kohsei Kudo¹, Yong Liu², Kenji Takahashi³, Kohetsu Tarusawa¹, Dong-Liang Hu³, Ikuo Kashiwakura¹, Hiroshi Kijima⁴ and Akio Nakane³

¹ Department of Radiological Life Sciences, Division of Medical Life Sciences, Hirosaki University Graduate School of Health Sciences. 66-1 Hon-Cho, Hirosaki-Shi, Aomori-Ken 036-8564 Japan.
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² Particle Radiation Oncology Research Center, Research Reactor Institute, Kyoto University. Kumatori-cho, Sennan-gun, Osaka 590-0494, Japan.

³ Department of Microbiology and Immunology, Hirosaki University Graduate School of Medicine. 5 Zaifu-Cho, Hirosaki-Shi, Aomori-Ken 036-8562, Japan.

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Purpose: The treatment of radiation-induced intestinal injury is difficult and effective treatments are currently unavailable. Developing new treatments for radiation-induced intestinal injury is important. We have previously reported that embryonic stem cells (ESCs) transplanted directly into the wall of irradiated intestine show colonization and differentiation. However, transplantation of ESCs did not influence survival rates or changes in body weights of mice with radiation-induced intestinal injury. The present study investigated whether transplantation of mesenchymal stem cells (MSCs) could prevent radiation-induced intestinal injury.

Methods: Intestines of female nude mice (ICR nu/nu) were irradiated at a single dose of 30 Gy (X-ray 150 kV, 5 mA, with 0.5 mm Al filters, at a dose rate of 1.9 Gy/min). Transplantation of male MSCs (C57BL/6n) was then immediately performed into the wall of the irradiated intestine by direct injection for the irradiation + MSCs group. For 13 days after irradiation, mice were weighed daily and survival was recorded. From 13 to 27 days after irradiation, intestines of mice were obtained to assay histological changes by staining with hematoxylin-eosin and Masson trichrome.

Results: Mean body weight was significantly higher in the irradiation + MSCs group than in the irradiation-only group from 8 days after irradiation. In addition, survival rate was significantly higher for the irradiation + MSCs group than for the irradiation-only group from 5 days after irradiation. Histological observation showed that intestines of irradiation + MSC-transplanted mice were thick in the submucosal and muscle layers, and had almost fully recovered from radiation-induced intestinal injury by day 27. Specifically, ulcerated areas in intestines of the irradiation + MSC-transplanted mice were narrower by 13 days after irradiation and fewer in number by 27 days compared to the irradiation-only group.

Conclusions: These results suggest that transplanted MSCs may play important roles in preventing radiation-induced injury and may offer a new method for treating radiation-induced intestinal injury. The protective mechanisms provided by transplanted MSCs warrant further study.
Recovery of the hematopoietic system after murine allogeneic umbilical cord blood transplantation

Hideaki Sato, Kyoko Ito, Koichi Ito

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Background: Umbilical cord blood cell (UCBC) transplantation has been applied for treatment of not only various hematological diseases but also accidental high-dose total-body radiation exposure. In clinical situations, a perfect major histocompatibility complex (MHC) match cannot be expected in UCBC transplantation, and the treatment is based essentially on non-related donor-recipient combinations. Although the low content of mature T cells allows the use of even MHC-mismatched UCBCs, the extent to which lymphocytes derived from MHC-mismatched UCBC transplantation recover their immune function is still unclear, due to the lack of convenient animal models.

Objective: In this study, we examined the differentiation, maturation, and function of lymphocytes derived from UCBC-hematopoietic stem cells in a fully MHC-incompatible combination utilizing a murine model system developed in a previous study.

Methods: Eight-Gray-irradiated RAG2(-/-)BALB/c [H-2d] mice were injected with three different doses of UCBC, which had been depleted of mature T cells, from green fluorescent protein (GFP)-transgenic C57BL/6 [H-2b] mice. Over 16 weeks after transplantation, successful reconstitution of immune cells was demonstrated by flow cytometric analysis. In addition, the function of T cells and B cells that had developed in the recipient mice was evaluated by examining the rejection of skin grafts from third-party donors and production of antibody against intraperitoneally injected 2,4,6-trinitrophenyl (TNP) - keyhole limpet hemocyanin (KLH), respectively.

Results: After UCBC transplantation, phenotypically mature fluorescent cells of donor origin, including T cells, B cells, monocytes and granulocytes, were observed in the recipients’ peripheral blood. Development of UCBC-derived T and B cells was also detected in the thymus and bone marrow, respectively, suggesting that lymphocytes that had developed from UCBC achieved normal maturation in lymphoid organs, even when MHC-incompatible combinations were used. Functional analysis demonstrated that allogeneic UCBC-transplanted mice accepted skin grafts from both BALB/c and C57BL/6 mice. However, these chimeric mice completely rejected skin grafts from third-party C3H/HeJ [H-2k] mice, indicating that both CD8+ killer and CD4+ helper T cells were functionally mature. Furthermore, TNP-KLH-immunized UCBC-transplanted mice produced both TNP-specific IgM and IgG antibodies. These results demonstrating the ability of recipient mice to develop antibody responses to T-dependent antigen with Ig-class switching confirmed that both B cells and CD4+ helper T cells derived from allogeneic UCBC were immunologically competent.

Conclusion: In terms of potential clinical application, our observations indicate that allogeneic UCBC transplantation can allow recovery of the normal hematopoietic system in patients who have been accidentally exposed to radiation.
Correlations of cell surface antigens with the individual differences of radio-sensitivity in human hematopoietic stem/progenitor cells

Satoru Monzen, Naoki Hayashi, Kenji Takahashi, Ikuo Kashiwakura

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The in vitro radio-sensitivity of human hematopoietic stem/progenitor cells (HSPCs) has been investigated in previous studies. However, little information has been reported to date with respect to the relationship between the heterogeneity of HSPCs and the individual differences of their radio-sensitivities. This understanding can predict the hematopoietic recovery from radiation exposure as well as the extent of radiation damage in hemaopoiesis. In addition, a diagnosis of the specific radio-sensitivity in patients who are suffering from malignant diseases allows radiation therapy and/or chemotherapy can thus be performed more effectively. Therefore, an understanding of the individual radio-sensitivity of HSPCs is very important.

In the present study, we examined the relationship among cell surface antigens, clonogenic potential and radiation survival, in order to characterize the individual differences of radio-sensitivity in human HSPCs. The expressions of CD34, CD38, CD45RA, CD110 and Tie-2 (tyrosine kinase with immunoglobulin and the epidermal growth factor homology domains 2), early differentiation pathway-related antigens in hematopoiesis, were analyzed on the surface of HSPCs enriched by CD34 antigen prepared from human placental/umbilical cord blood. The significant positive relationship was observed between CD38 antigen and CD110 and Tie-2, respectively. The number of megakaryocytic progenitor cells correlated negatively with the rate of Tie-2+ cells. While, no significant relationship was observed in almost all cases among the antigens and the number of colony-forming cells CFC. With respect to the radio-sensitivities, the expression of Tie-2 antigens correlated significantly with the surviving fraction of CFC, suggesting that the individual radio-sensitivity of CFC is predictable with respect to the Tie-2 rate of HSPCs to some extent. In addition, the number of progenitor cells correlated strongly with its surviving fraction. These results suggest that the individual radio-sensitivity of HSPCs is predictable with respect to the number of progenitor cells to some extent, especially, its dependency on the presence of immature HSPCs such as Tie-2+ cells.
Radiation Emergency Medical Preparedness in Japan and a Criticality Accident at Tokai-mura

Makoto Akashi

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In Japan, the system of radiation emergency medical preparedness has been established for nuclear facilities such as power plants, reprocessing facilities and research reactors. Hospitals involved in this system are classified into three levels. The primary level hospitals are located near nuclear facilities and the secondary level hospitals are usually local general hospitals such as universities and national hospitals. As the third level of hospitals, the Hiroshima University and the National Institute of Radiological Sciences (NIRS) play their roles in the West and the East Japan, respectively. The primary role of these hospitals in radiation accidents is to determine effects of radiation on the victims and also the public people by assessment of radiation dose or measurement of internal and/or external contamination. NIRS has been also designated as a national center for radiation emergency medical preparedness and the victims highly contaminated with radionuclides are transported to NIRS. The whole body exposure to radiation, on the other hand, causes damage to not only a single organ but also multiple organs in nature. Therefore, treatment by experts in various medical fields is required. Moreover, it is difficult for a hospital to treat two or more victims heavily exposed at the same time. NIRS has constructed a collaborative system with extramural specialists. This is the Medical Network Council for Radiation Emergency established in July of 1999. This council consists of experts from more than ten major hospitals and institutes, who will cooperate to conduct treatment, especially treatment for radiation burns, severe bone marrow failure, and gastrointestinal injuries. In the criticality accident which occurred at Tokai-mura in 1999, treatment of three victims was carried out at NIRS and hospitals of this network. We have also established the Network Councils for Chromosome Analysis for dose assessment. The Network Councils for Physical Dosimetry has been built to provide quick and precise dose estimation by radiation measurement and/or re-construction of the accident. We are now constructing the regional medical network system for radiation emergency in the local governments. The aim for construction of the network is to share information on the radiation accident from the nuclear facilities for these local hospitals and also to receive patients smoothly or to send patients to the third level of hospitals. In the symposium, details of these network systems and also lessons learned from the Tokai-mura accident will be presented.
Overview of NIRS Educational Programs on Radiation Emergency Medical Preparedness

Hideo Tatsuzaki

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The National Institute of Radiological Sciences (NIRS) has a function of education and training for professionals as one of its missions. It has a designated training facility and accommodations for participants. The institute conducted many training courses in the field of radiation emergency medicine and related subjects both for Japanese and foreigners.

NIRS organized many courses for foreigners, sometimes in cooperation with several organizations, such as the International Atomic Energy Agency, the World Health Organization, or the Japanese Nuclear Safety Commission. From 2001 to 2009, NIRS has organized 11 international training courses or workshops. About 240 overseas professionals, mainly from Asian countries, have been participated in these meetings. They were mainly medical staffs, such as medical doctors or nurses, health physicists, or administrators who were responsible for national system of radiation emergency medicine. These courses will be presented.

The institute also organized many courses for Japanese professionals from prefectures near nuclear facilities until last year, in order to prepare accidents in nuclear facilities. In this year, we are planning to start new courses with wider perspectives. The new courses are focused on radiation accidents and radiation terrorisms in addition to accidents in nuclear power plants. We plan two types of courses: one for medical staffs (hospital management) and another for first responders (pre-hospital management). Radiation is used in many places other than nuclear power plants. Accidents can be happen anywhere. More over, a threat of nuclear or radiological terrorism is emerging in the world. Thus, these new educational courses are highly expected.
Chromosome abnormality as a genetic indicator for radiation dose assessment and carcinogenesis

Mitsuaki A. Yoshida

Biodosimetry Section, Department of Radiation Dose Assessment, Research Center for Radiation Emergency Medicine, National Institute of Radiological Sciences, 4-9-1 Anagawa, Inage-ku, Chiba 263-8555, Japan.

Irradiation induces many types of chromosome abnormalities in cells. Particularly, dicentric and centric ring are specific and dose dependent response to radiation. Therefore, these chromosome abnormalities are used as a biological marker for dose estimation in exposed individual. Generally, the dose estimation is important to determine the medical treatment for the exposed person. In case radiological accidents occur, the dose estimation should be performed in the exposed individual as soon as possible. Dose estimation with dicentric assay is known as the gold standard method and is the most reliable biological marker for radiation exposure.

On the other hand, most solid tumors, leukemia and lymphomas have acquired, nonrandom chromosomal abnormalities, which in some cases are sufficiently specific to be diagnostic as a marker for a specific cancer and analyze carcinogenesis. The well known Philadelphia chromosome, translocation between chromosomes 9 and 22, is a specific genetic marker to determine chronic myelocytic leukemia (CML). Moreover, identification of such nonrandom chromosome alterations specific to each human cancer has contributed to the isolation of oncogenes and tumor suppressor genes associated with the cancer development. Thus, the chromosome abnormalities give more important genetic information to the field of life science, especially radiation dose assessment and cancer development.
Experimental Studies on Biological Effects of Continuous Exposure of Mice to Low-Dose-Rate Gamma-Rays in a Special Reference to Transgenerational Effects and Biological Defense System

Yoichi Oghiso

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We demonstrated in a large-scale life-span study that a significant life-shortening due to earlier neoplastic death is observed in mice after continuous gamma-irradiation for approximately 400 days with a high dose of 8000 mGy at a low-dose-rate of 20 mGy/day, while no significant difference in life span was found in mice irradiated with a low dose of 20 mGy at a low-dose-rate of 0.05 mGy/day. Based on such results obtained from the life-span study, we currently investigate on the biological effects of continuous low-dose-rate radiation exposures in mice as follows;

The first one is on the transgenerational effects to determine whether or not the effects of long-term, paternal gamma-irradiation at low-dose-rates could be inherited by the progeny mice. The second one is on the biological defense system to clarify whether or not changes in the immune system and metabolisms could lead to development and progression of neoplasms after continuous gamma-irradiation at low-dose-rates. The third one is on the tumor-related genes to clarify alterations of tumor-related genes and their expression could lead to generation and development of neoplasms after continuous gamma-irradiation at low-dose-rates. The fourth one is on the biological dosimetry for low-dose-rate and low-dose radiation exposures to establish the methodology for accurate and quick estimation of exposure doses using chromosomal aberrations of peripheral lymphocytes after low-dose-rate and low-dose radiation exposures. Here, the current research topics obtained from the first and second research projects will be presented. All the works were performed under contract with Aomori Prefectural Government, Japan.
Chromosome Aberration Rates in Splenocytes and Genomic Alterations in Malignant Lymphoma from Mice Long-Term Exposed to Low-Dose-Rate Gamma-Rays

Kimio Tanaka

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Chronically exposed individuals to very low-dose radiation, such as nuclear workers, medical radiologists and residents in high-background areas have chromosome aberrations with higher incidences than non-exposed individuals, although the relationship between chromosome aberrations rates and dose-rate is not well-known. Epidemiological studies of human populations have uncertainties and are influenced by confounding factors such as smoking. We analyzed serially chromosome aberration rate in spleen cells of long-term gamma-irradiated C3H mice up to 400 days and 615 days, respectively, at the low-dose rates (LDRs) of 20 mGy/22h/day (0.91 mGy/h) and 1 mGy/22h/day (0.045 mGy/h), and compared with those induced by irradiation at 400 mGy/22h/day. Dicentrics and translocations increased almost linear at the LDR of 20 mGy/22h/day irradiation and clear dose-rate effects were found in dicentric chromosomes among these dose rates used in the present study. Clonal cells such as trisomy 15 increased rapidly more than 4000 mGy at the LDR of 20 mGy/22h/day, which might be associated with lymphomagenesis. Furthermore, B6C3F1 mice irradiated for 400 days with LDR at 20 mGy/22h/day had shorter mean life spans than non-irradiated controls. This life span-shortening was attributable to earlier death due to all malignancies including malignant lymphomas (ML) in irradiated mice. To elucidate the molecular mechanisms of murine lymphomagenesis by LDR irradiation, genomic copy changes were analyzed by microarray-based comparative genomic hybridization (CGH) analysis. The genomic profile showed a high frequency of trisomy 15 in both MLs developed from irradiated and non-irradiated mice. By comparing the frequency of aberrations, partial losses of chromosome 4 and 14 were significantly higher in MLs from irradiated mice, and partial gains on chromosomes 12, 14 and X were in those from non-irradiated mice. Candidate genes for lymphomagenesis contained in these regions were \textit{Akt1}, \textit{Bcl11a}, \textit{c-myc}, \textit{Cdkn2a Cdkn2b}, \textit{Tp73} and so on. These findings suggest that the long-term LDR irradiation could influence genomic changes and promote development of lymphoma. This study was performed under contract with Aomori Prefectural Government, Japan.
Radiation Detection and Measurement in Patients Contaminated with Alpha Emitters

Takumaro Momose, Osamu Kurihara, Chie Takada, Sadaaki Furuta

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Management of patients contaminated with radioactive material on site is one of important issue in nuclear emergency preparedness at nuclear fuel cycle facilities. Especially in case of nuclear accident concerned to contamination with radionuclide which emits alpha particle, radiation detection and measurement of surface radioactive contamination in human body and/or internal contamination will give important information affecting the operation of medical treatment. In addition to preparedness at on site, medical personnel at off site hospital concerned to nuclear emergency must be trained in the detection and measurement of patient contamination in order to prevent uncontrolled exposures of hospitals and personnel.

The purpose of this presentation is to provide radiological information focused on alpha emitter. The basic principle of radiation control at plutonium facility such as characteristics of plutonium and relevant radionuclide which are operated in nuclear fuel cycle facilities is introduced and potential radioactive contaminations in accident is discussed. As a practice, decontamination procedure of skin at Tokai Reprocessing Plant and some of the operating principles and applications of various radiation detection and measurement instruments for contamination control and occupational monitoring for internal contamination will be introduced. Special methods of measurement for alpha emitters and basic techniques for performing radiological monitoring for contaminated patient such as radio autography, nasal swab, in vivo and in vitro analysis for plutonium and uranium will be described. Internal dose calculation code was originally developed in order to estimate dose reduction by chelation therapy in case of accidental intake of plutonium. Some actual contamination incidents experienced in JAEA facilities will also be discussed.
In Rokkasho-mura, Aomori prefecture, Japan Nuclear Fuel Limited (JNFL) now has operated three types of nuclear fuel cycle facilities: Uranium Enrichment Plant, Vitrified Waste Storage Center, and Low Level Radioactive Waste Disposal Center, and is also focusing on Reprocessing Plant operation during active test. The number of radiation workers in these facilities totaled about 7,000 workers in 2008.

JNFL has prepared a program of radiation emergency medicine under the plan of Aomori prefecture and the Nuclear Safety Commission in case of radiation incident. There are our clinics in the reprocessing plant site and in the Obuchi area outside a site in which one doctor and five nurses are working.

JNFL concluded the agreement about radiation emergency medicine with three regional hospitals (Primary Hospital: Aomori Rosai Hospital, Secondary Hospital: Hachinohe City Hospital, Tertiary Hospital: Hirosaki University School of Medicine & Hospital), because of special medical treatment, and made the agreement about Fire-fighting including emergency conveyance with the local fire station (Hokubu Kamikita Fire Department). We are training periodically with those organizations and it is maintained the system which can be respond quickly and correctly.

It is an important issue to convey a patient quickly on influencing a patient’s life. In the future, it will be desirable to convey a patient in an emergency by a doctor helicopter that Aomori Prefecture began operation of recently.
DTPA Administration Methods for Accidents of α Particle Contamination

Yutaka Jin
Emergency Medicine Team, Japan Nuclear Fuel Ltd

Diethylene triamine pentaacetate (DTPA) is a calcium or zinc salt that is specifically used for treating people who have been internally contaminated with plutonium, americium and curium. The DTPA administration protocol using newly designed electric mesh nebulizer for contaminated workers was discussed.

DTPA administration methods include inhalation, intravenous administration and application to wound. As inhalation is the easiest among these administration methods, it enables administration at an early stage in the radiation controlled area.

In the event of plutonium inhalation, a nose smear test of radionuclides is performed. This method measures the amount of radioactive material adhering to a filter paper with which the nostril is swabbed. Although this method is easy to perform, the calculation of intake is inaccurate. Therefore, in the event that nose smear test shows any significant count, DTPA inhalation is conducted immediately. 50mg of DTPA is administered by inhaling it for 1 minute. DTPA solution is sticky, but electric mesh nebulizer can produce sufficient mist without dilution. As it produces mist without leaking even if turned upside down, it is usable in confused circumstances.

Following the nose smear test, lung monitor and bioassay testing are performed. A lung monitor is a device that detects gamma rays and X rays by germanium semiconductor. Bioassay is a method to analyze urine and stool. Additional administration of DTPA by injection is based on these data of lung monitor and bioassay.

Treatment with DTPA for contaminated workers should be made as early as possible, because the effectiveness of treatment can drop dramatically within a few hours. A promptly administered DTPA aerosol would have the advantage that plutonium would be chelated in the respiratory tract, thus minimising subsequent deposition in systemic tissues. Moreover, combined treatment involving early inhalation of DTPA followed by repeated intravenous injections is likely to be the most effective treatment for workers who have accidentally inhaled plutonium and americium.
Shandong Radiation Exposure October 21, 2004

Yutaka Jin¹, Xiaohua Chen²

¹ Emergency team, Japan Nuclear Fuel Ltd
² Beijin Institute of Radiation Medicine

Accident Summary:

It was at 5:30 in the evening on October 21, 2004 when the radiation source control was short-circuited that caused aberrant conditions while two workers from a food irradiation plant in Shandong engaged in vegetable freshness-preserving process using radiation source Co60 (0.3 million curies of radiation). The radiation source control failed to lower to a safety position. Patients A and B transported vegetables in the field while the radiation source was in action (1.5 meters above the ground) and worked for a few minutes 0.8 to 2.0 meters away from the radiation source before walking away from the field.

With Patient A, the first symptoms appeared 3 minutes after getting out of the field. The following symptoms had developed: nausea attended with continuous abdominal pains, vomiting, headaches, languor, and bleariness. Vomiting 7 times in a row and no diarrhea was observed.

With Patient B, the first symptoms appeared 10 minutes after getting out of the field. The following symptoms had developed: nausea attended with continuous abdominal pains, vomiting, headaches, languor, and bleariness. Vomiting 5 times in a row inducing gastric emptying and diarrhea twice was observed.

The said two patients were admitted to the hospital at 7 p.m. on October 21. Findings on admission with the patients included drowsiness, mental instability, body temperature of 38.1 to 39.2°C, heart rate of 98 beats a minute, blushing face and hands, and parotid and abdominal tenderness. The symptoms slightly subsided in response to appropriate medical treatment, but abdominal pains and mental instability persisted. The patients were transferred to the Beijing Institute of Radiation Medicine Hospital at midnight on October 24, 2004.

Reference Dose:

Patient A
Physical dose: 20 to 25Gy; Biological dose: 12 to 25Gy; Exposure dose integrated evaluation: 16 to 25Gy

Patient B
Physical dose: 9 to 15Gy; Biological dose: 8 to 12Gy; Exposure dose integrated evaluation: 8.5 to 13.5Gy

Clinical Therapy:

A hematopoietic stem cell transplant was practiced due to a relatively large quantity of exposure and a slim chance of hemopoiesis self-recovery. The first day at the hospital, (+4d) HLA matching was carried out to identify the degree of matching between the patients and their respective family members (donors). As to Patient A, his 51-year-old sister: DR/DQ matched and A/B loci half-matched; as to Patient B, his 52-year-old brother: HLA fully matched. The following table shows the pre-transplant processing plan.
Variations in the white blood cell count before and after hematopoietic stem cell transplant are presented in graphical form below.

**Variation diagram of WBC count before/after transplant**

![Variation diagram of WBC count before/after transplant](image)

**Variations in three homologous series hemogram in sample blood**

![Variations in three homologous series hemogram in sample blood](image)
Patient A was diagnosed as having severe lung infections with chest x-rays and CT scans that he underwent several times eight days after the transplant. It was clinically-convincing fungal infections and microbism of the lungs, which led to the use of amphotericin B and itraconazole as an antifungal agent and of Tienam and Vancocin as an antibacterial agent in treatment. These drugs, however, produced little effect, which allowed the patient to develop complications of hypoactivity in lungs, heart, kidney, and liver. Although the patient was attached to a respirator by cutting open his windpipe 30 days after the exposure, he died of a multiple organ failure on the 33rd day despite a life-saving measure.

Patient B had been suffering from severe lung fungal infections since the 17th day after the exposure and later was diagnosed as Trichosporon asahii and Aspergillus terreus in sputum culture examinations conducted several times. In combination with Caspofungin, Amphotericin B, itraconazole, and fluconazole, antifungal treatment improved fungal infection noticeably. Treatment using antibacterial agents including Tienam, Vancocin, and piperacillin and antiviral agents including ganciclovir enabled control of microbism to some extent despite septic symptom (Gram-positive and -negative sepsis), and cytomegalovirus test turned out negative.

However, the patient showed signs of his lung infections, total-body radiation injury, and organ functions worsening, which heavily limited his respiratory function and developed respiratory distress syndrome. He was attached to a respirator by cutting open his windpipe 45 days after the exposure. Consecutive occurrences of complications, such as arrhythmia, cardiac failure, hepatic failure, kidney failure, gastrointestinal paralysis, and intestinal obstruction, caused unstable vital signs and brought him to a low oxygenation level and an exaggerated hypotensive state. On the 73rd day, the patient went into cardiac arrest and developed third-degree AV block. AV block failed to be treated with cardiac pacing, and he died of a multiple organ failure at 9:10 p.m. on January 4, 2005 (75th day) despite a life-saving measure.
A New Therapeutic Approach for Radiation Burns combining Surgery and Mesenchymal Stem Cell Administrations: About four cases

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The physiopathological mechanisms of severe radiation burns are well described and therapeutic process is well codified but very difficult with an important functional and vital risk. We present four patients with local radiation burn and propose a new therapeutic approach combining surgery and local stem cell therapy. It’s a preliminary report but the results are very promising.

The first patient had local radiation burns of left fingers and left buttock. We performed early excision of the irradiated part of the buttock after dosimetric reconstruction. We covered the buttock and the fingers with full thickness skin graft and autologous Mesenchymal Stem Cells were locally administrated in the lesion at the same time.

The second patient had a very important radiation-induced skin necrosis located to the left arm from the shoulder to the elbow. The surgical procedure used a pedicle latissimus dorsi muscle flap and a proximal forearm antebraclial flap after a very large excision of skin and triceps muscle. Several Stem Cell administrations were combined to the surgery after many bone marrow collections.

The third patient had a local radiation burn of the hands. Full thickness skin grafts were combined with local stem cells administrations.

The fourth current case presents a local radiation-induced burn of the limb and is hospitalized and treated in our Hospital following the same procedure.

All these cases are radiation accidents occurred in the world: Chilli, Senegal, Tunisia and Equator.

We obtained a complete and stable healing in the three first cases. Stem cell therapy using autologous expanded MSC has to be considered as an adjuvant treatment of the surgery corresponding to excision of necrosis tissues and flap reconstructions.

Our results demonstrate that this new therapeutic procedure of local radiation burns using surgery and local stem cell therapy is very promising. We believe that this innovative approach could improve the treatment of local radiation burns in term of functional and vital results.
Mesenchymal Stem Cells as Drug Cells for Radiation Burn Treatment

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Local radiation syndrome is marked by necrosis that may extend to the deep subcutaneous structures. Today, treatment is surgery, excision, graft and flap with sometimes bad results. It has been suggested that Mesenchymal Stem Cells (MSC) therapy could be used in order to treat numerous tissue lesions. We have performed a novel therapeutic approach of local radiation syndrome by using local autologous MSC therapy combined to surgery. For this purpose, autologous bone marrow cells were collected from the unexposed iliac crest. For GMP production, MSC were expanded in a closed system (MacoPharma partnership) containing an innovative serum free medium supplemented with human platelet lysate as previously described (Doucet et al., \textit{J. Cell Physiol.}, 2005). Quality control assays evidenced that expanded cell population retained typical MSC characteristics and did not exhibit chromosomal abnormalities. As previously demonstrated, MSC produced many cytokines and growth factors which could have a critical role in improving the healing process by counteracting the local inflammatory waves and by promoting the autologous skin engraftment.

We believe that MSC act as drug cells delivering \textit{in situ} in the lesion growth factors which contribute to the healing of the lesion. We have also demonstrated that after \textit{in vitro} cell activation, the conditioned medium of MSC exhibited a similar effect on wound healing than that obtained with freshly expanded MSC. In case of caryotypic abnormalities occurring after \textit{in vitro} MSC expansion, the use of MSC conditioned medium could be considered as a relevant alternative of MSC therapy. Other sources of MSC such as adipose tissue, gingival mucosa are also taken in consideration in view of setting up an allogeneic stem cell bank.
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