

The 2nd International Symposium Phoenix Leader Education Program (Hiroshima Initiative) for Renaissance from Radiation Disaster

- Suggestion for the Renaissance
from Radiation Disaster -

“放射線災害復興への提言”

HIROSHIMA

February. 10-11, 2013

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Japan*

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放射線災害復興を推進するフェニックスリーダー育成プログラム
第2回国際シンポジウム「放射線災害復興への提言」



広島大学長 浅原利正

開会式挨拶

広島大学大学院の『放射線災害復興を推進するフェニックスリーダー育成プログラム』は、昨年10月から開講され、第1期大学院生8名が入学し、博士課程教育リーディングプログラムが、本格的に動き出しました。

ご存知の通り、広島大学は世界で最初の被爆地広島市に開学した総合大学として、被爆体験とその研究成果を基に、これまで放射線災害に係る学術・医療面から、国内外の放射線災害復興の支援に取り組んでまいりました。

2011年3月11日の東日本大震災とともに起った福島第一原子力発電所事故は、原子力発電所という巨大管理システムの崩壊が、原子力発電施設だけでなく、放射線災害に対する社会システムの脆弱さを露呈し、放射線への安全・安心の問題は、広範囲の学術領域の総合的な連携により解決しなければならないことも明らかになりました。

さらに、世界各国に数多く設置されている原子力発電所の事故の可能性を考えると、被曝災害の学術的知見や行政的施策を背景に、放射線災害に対して実践的な対応のできるグローバル人材の育成が愁眉の急となっています。この点で、本学の『放射線災害復興を推進するフェニックスリーダー育成プログラム』は、放射線災害対応の国際的人材養成のために重要な教育プログラムです。

本国際シンポジウムは、放射線災害への対応から社会復興までの幅広い領域の国際的な研究者の講演、並びに本プログラム大学院生の研究成果を、一般に公開する機会として定期的に計画しており、今回が2回目に当たります。

本シンポジウムを通して、放射線災害に対する幅広い研究者の知見が多く、多くの研究者の共通理解となり、本学のリーディングプログラムの人材養成の意義を、ご参会の皆様方にご理解いただけることをこころより願っております。

Date: February 10 (Sun), 2013
Venue: International Conference Center Hiroshima

Phoenix Leader Education Program for Renaissance from
Radiation Disaster: 2nd International Symposium
“Suggestion for Renaissance from Radiation Disaster”



Opening Remarks

Toshimasa Asahara, President of Hiroshima University

Hiroshima University Graduate School’s Phoenix Leader Education Program for Renaissance from Radiation Disaster opened in October 2012 with eight graduate students enrolled in the inaugural class, signifying the full-scale launch of the Ph.D. level “Leading Graduate Education Programs” offered at Hiroshima University.

As you all know, Hiroshima was the world’s first city to come under a nuclear attack. As a comprehensive university established in this city, Hiroshima University has built upon Hiroshima’s A-bomb experience and accumulation of research on the subject to engage in post-radiation disaster recovery assistance both at home and abroad, in academic and medical fields pertinent to radiation disasters.

The Fukushima Daiichi Nuclear Power Plant accident triggered by the Great East Japan Earthquake on March 11, 2011 exposed—in the spectacular collapse of the behemoth of a control system that makes up a nuclear power plant—not only the fragility of such facilities but also how vulnerable current social systems are to radiation disasters. It was also made apparent that comprehensive and extensive interdisciplinary partnership is essential for addressing radiation safety and security.

Considering the risk of accidents posed by the world’s numerous nuclear power plants, it is critically urgent that we develop global talent capable of responding practically to radiation disasters, on the back of academic expertise and public initiatives on radiation disasters. It is in this context that Hiroshima University’s Phoenix Leader Education Program for Renaissance from Radiation Disaster, a program for nurturing international experts in radiation disaster response, plays a key role.

This is the second of our international symposiums held regularly to share with the public not only research findings of graduate students enrolled in the Phoenix Leader Education Program but also lectures by international experts specializing in areas ranging from radiation disaster response to social rehabilitation.

I sincerely hope that the symposium will help the participants’ extensive radiation disaster expertise become shared knowledge among the many people who are studying the subject, and convince all of you here today of the rationale of the human resource development carried out by Hiroshima University’s “Leading Graduate Education Programs.”

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General Information

Data

February 10-11, 2013

Venue

International Conference Center Hiroshima

1-5 Nakajima-cho, Naka-ku, Hiroshima 730-0811, Japan

Phone: +81-82-242-7777 Fax: +81-82-242-8010

Language

English and Japanese

Hosted by

Organization for the Leading Graduate Education Program, Hiroshima University

放射線災害復興を推進する フェニックスリーダー育成プログラム

放射線災害による人と社会と環境の破綻からの復興を担う
グローバル人材養成

本プログラムでは、原爆からの復興を支えた広島大学の実績と経験を生かして、分野横断的・実践的学問領域である「放射線災害復興学」を確立し、放射線災害からの復興の核となる「放射線災害から生命を守る人災」、「放射能から環境を守る人材」、「放射能から子どもと社会を守る人材」を育成します。5年もしくは4年一貫の徹底した人材育成カリキュラムにより、放射線災害に適切に対応し、明確な理念の元で復興に貢献できる判断力と行動力を有した、国際的に活躍できる分野横断的統合的グローバルリーダー（フェニックスリーダー）を輩出します。

（文部科学省「博士課程教育リーディングプログラム」 平成23年度採択プログラム）

Phoenix Leader Education Program (Hiroshima Initiative) for Renaissance from Radiation Disaster

Develop global human resources who are expert in the recovery
of people, society and the environment
from damage caused by radiation disaster

This program establishes “Radiation Hazard Recovery Studies” as an interdisciplinary and practical discipline, based on Hiroshima University’s experience and achievements in supporting recovery from the atomic bomb. The program will develop personnel with the skills to “protect human lives from radiation hazards”, “protect the environment from radioactivity”, and “protect children and society from radioactivity”. Graduates from the program will become core leaders in situations requiring recovery from radiation hazards. The 5-year or 4-year integrated curriculum is designed to develop interdisciplinary and comprehensive global leaders (Phoenix Leaders) who can act appropriately in circumstances of radiation hazards, and who can contribute to the recovery with leadership based on a clear philosophy.

(Ministry of Education, Culture, Sports, Science and Technology – MEXT
“PhD Leading Program” accepted for 2011FY)

Program

**The 2nd International Symposium on
Phoenix Leader Education Program (Hiroshima Initiative) for
Renaissance from Radiation Disaster**

“Suggestion for the Renaissance from Radiation Disaster”

February, 10-11, 2013

International Conference Center Hiroshima

February, 10, 2013, Room : Himawari

12:00- Registration

12:30-13:00 **Opening Ceremony**

Welcome Remarks

Tetsuji Okamoto (Program Director of Phoenix Leader Education Program)

Opening Remarks

Toshimasa Asahara (President of Hiroshima University,
Director General of Phoenix Leader Education Program)

Guest Remarks

Takakuni Ikeda (Director, University Promotion Division. Higher Education
Bureau, Ministry of Education, Culture, Sports, Science, and
Technology-Japan)

13:00-15:00 **Keynote Address**

Keynote Address I

Dr. Shinsuke Shimojo (Professor, California Institute of Technology)

Why did it look cheap and safe?

- Cognitive biases in group decision regarding energy economy and safety -

Keynote Address II

Dr. Rethy K. Chhem (Director, Human Health, IAEA)

**Creating new knowledge in Human Health within post-Fukushima context:
The International Atomic Energy Agency’s initiative**

15:00-15:10 **Break**

15:10-17:50 **Lectures**

15:10-15:40 **Lecture I : Dr. Jacques Lochard**

(Director, Nuclear Protection Evaluation Centre (CEPN))

**Rehabilitating Living Conditions after a Nuclear Accident:
Lessons from Experience**

15:40-16:10 **Lecture II : Dr. Tokushi Shibata**

(Senior Scientist, Chiyota Technol Corporation)

**Detailed investigation of radionuclides distributions caused by the
Fukushima Daiichi nuclear disaster**

16:10-16:40 **Lecture III : Dr. Seiichi Nohara**

(Executive Director, Center for Environmental

Biology and Ecosystem Studies, National Institute for Environmental Studies)

**Inventories of radionuclides in wetland ecosystems
in Fukushima Prefecture, Japan**

16:40-16:50 **Break**

16:50-17:20 **Lecture IV : Dr. Albert Lee Wiley**

(Medical and Technical Director, REAC/TS)

**Medical Management of Radionuclide Internal Contamination in Mass
Casualty Scenarios Involving Fission Products, Such as in Nuclear Power
Plant Accidents**

17:20-17:50 **Lecture V : Dr. Tom K. Hei**

(Professor and Vice-Chairman of Radiation Oncology, Columbia University Medical
Center)

Radiobiology in the Context of Radiation Protection During a Radiological Event

17:50-18:30 **Break and Photograph**

18:30-20:30 **Reception** Room : Cosmos 2

February, 11, 2013

9:00-10:20 **Poster Session** Room : Dahlia 2

10:40-12:20 **Panel Discussion** Room : Dahlia 1

Dr. Shinsuke Shimojo (Professor at California Institute of Technology)

Dr. Rethy K. Chhem (Director, Human Health, IAEA)

Dr. Kenji Kamiya (Program Coordinator of Phoenix Leader Education Program)

Uranchimeg Tsegmed (Program Student, Radiation Disaster Medicine Course)

Wim Ikbal Nursa(Program Student, Radioactivity Environmental Protection Course)

Mariko Komatsu (Program Student, Radioactivity Social Recovery Course)

“How can the science and technology contribute to the social construction for security and safety ?”

12:20-12:30 **Closing Ceremony** Room : Dahlia 1

Poster Awarding

Tetsuji Okamoto (Program Director of Phoenix Leader Education Program)

Closing Address

Kenji Kamiya (Program Coordinator of Phoenix Leader Education Program)

Abstracts

Keynote Address

and

Lectures

February, 10, 2013

13:00-17:50

International Conference Center

Hiroshima

Room : HIMAWARI

Keynote Address 1

Why did it look cheap and safe? - Cognitive biases in group decision regarding energy economy and safety -

なぜ安くて安全に見えたのか？

- エネルギー経済と安全性に関する集団意思決定とその認知バイアス -

Shinsuke Shimojo

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Introduction

The “Black swan” often refers to an unexpected big event¹. It has three distinctive features: 1) highly unlikely, 2) the impact being huge (either positive or negative), and 3) once it happens, it retrospectively appears “to have been well predictable.” Surprisingly (or not), the major nuclear disaster caused by 3.11 Fukushima tsunami (2011) qualifies well as such. Why did people commit to the nuclear energy in Japan as the “nest of earthquakes”? What made them blind to the huge risk? And what went wrong in their risk management? Whereas I am not an expert in nuclear technology nor its safety, I attempt to utilize my expertise in cognitive psychology and neuroscience to answer these questions, to prepare best for the future.

My working hypothesis

A single human brain shows various cognitive biases, often behaving irrationally, against the classical “ideal decision maker” who makes decisions to maximize benefit and to minimize risk. My working hypothesis, not yet fully supported, is the following - When it gets to a large-scale group decision (concerning energy policy or stock market trends, for instance), such biases are often enhanced to lead to a disaster (the severe accident at a nuclear plant, or the collapse of the bubble economy).

Cognitive biases

- 1.** Compulsive people, such as gamble-addicts, tend to accept a large potential damage in far future just to obtain a small, but immediate benefit^{2,3}. Credit card business which is more prevalent in “advanced” countries cashes ordinary people’s tendency which is a weaker version of the pathological compulsive behavior. Considering the large costs and risks that it leaves for the next generation, nuclear energy economy may crudely be regarded as such at larger (financial and temporal) scales. The “time discount factor” is larger for reward than punishment (eg. \$100 cash now is equivalent to \$80 next week; \$85 penalty is equivalent to \$100 next week)⁴, and it may pose a paradox, if one thinks more on the cost-benefit in the future. The mere fact, however, is that people (the government and companies) are too compulsive to think that far.
- 2.** People grossly underestimate the potential risks, due to a variety of factors. To begin with, people are intrinsically bad at dealing with uncertain events, evaluating risks only based on the data from the past¹.
- 3.** Not only a pain, but also a mere observation/imagination triggers neural response⁵, thus it tends to avoid it whenever possible. Careful and extended simulation of various scenarios of huge-scale disasters had been difficult as “out of imagination,” preventing appropriate preparations.
- 4.** People perceive only what they want to see, particularly when they committed to a notion (of the absolute safety of the nuclear power plant). For example, repeated small incidents at the plants have been taken as a sign of ultimate safety, as opposed to that of a real risk. Cognitive dissonance, subliminal priming, hindsight (postdiction)⁶, and escalating commitment to a failing course of action⁷, are some of the keywords.
- 5.** Daily safety managements/regulations are highly susceptible to habituation. There is laboratory evidence that when pushing a little towards the risk is rewarded each time, people tend to push until it explodes⁸.
- 6.** At the moment of urgent risk management (eg. encountering a tsunami), people tend to be in a panic mode. Their behavior will be stereotypical, emotional and irrational, becoming fundamentally inconsistent with the requirements for varying disaster scenarios with such a complicated system. Moreover, people will be “choked” under time and mental pressures⁹. Massive emergency drills would help only to a limit, for several basic reasons.

Discussion and Conclusions

Thus as I speculated, group decision at a large scale tends to have risky biases which are exaggerated from the individual level. It may be partly due to inappropriate social systems which have not been designed to serve as a safety net against such biases. Overall, the psychological “shared reality” have deviated from the objective reality concerning costs and risks. In Japan, additional psychological factors related to cultural differences related to in-group/out-group modulation of behavior may have contributed negatively.

As for the first step towards restoration and beyond, we do need to raise a keen awareness of them, to aim for the systems which are more flexible and robust.

References

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[PROFILE] Shinsuke Shimojo (Professor, California Institute of Technology)

Professor Shimojo was born in Tokyo of 1955. His major fields are cognitive psychology and cognitive neuroscience. He graduated from Tokyo University at 1978, and he received his Ph.D in experimental psychology from MIT in 1985. Since 1998 he has been a professor of Biology Division –Computation & Neural Systems at California Institute of Technology, through an associate professor at Department of Psychology / Department of Life Sciences, Graduate School of Arts & Sciences, Tokyo University. He has published uncountable various articles and provided lectures in various international symposium. His representative Japanese books, which have given a strong impact to our Japanese, are follows: “Beginning to See - *Genesis of Mind, and The New Infant Science*” (1988), “Adventure of Vision - From Illusions to Sciences” (1995), “Subliminal mind – implicit aspects of the human” (1996), “What is ‘consciousness’ – Plasticity of brain, and perceptual illusions” (1999), “Subliminal Impact – Contemporary world, emotional and implicitly cognitive” (2008). He won the best presentation award in division of pattern recognition and modeling of perception from Japanese Society of Cognitive Science (1991), Suntory Prize for Publication in Social Sciences and Humanities (1999), Tokizane Memorial Award from Japanese Neuroscience Society (2004) and Nakayama Grand Prix from Nakayama Press (2008). If you want to see his detailed curriculum vitae, check the following website :

<http://neuro.caltech.edu/page/>

Keynote Address 2

Creating new knowledge in Human Health

within post-Fukushima context:

The International Atomic Energy Agency's initiative

Rethy Chhem and Soveacha Ros

Division of Human Health,
International Atomic Energy Agency, Vienna, Austria



The International Atomic Energy Agency (IAEA) has a distinctive mandate to “accelerate and enlarge the contribution of atomic energy to peace, health, and prosperity throughout the world”. The IAEA recognizes education and research as a key component of “readiness, response, and recovery” with respect to a major nuclear accident. In this paper, we address an ongoing process of Division of Human Health (NAHU) of the IAEA in calling for a more comprehensive Science and Technology Studies (STS) approach to creating and mobilizing new knowledge into collaborative education and research programmes and policy implementations as based on the post-Fukushima recovery context. NAHU plays an instrumental role in this process. We discuss an output from a consultancy meeting on “Global radiation medicine: Educational challenges for academia” as grounded in a focus group methodology. As a result of the meeting, two STS-oriented projects are being implemented. The first project aims to enhance global radiation medicine education by building capacity of health professionals and medical students.

The second project aims to strengthen research cooperation in radiation disaster medicine including post-traumatic stress disorders. NAHU involves both international and Japanese STS and disaster studies experts as a way to integrate outsider and insider perspectives on the Fukushima accident in order to activate the STS approach to construct new knowledge in Human Health for health professionals, medical students, and specialists from relevant fields such as sociology, anthropology, and psychology. To fill in the knowledge gap in this field, new knowledge creation can trigger “thick description” to add value to the emerging academic

responses to the Fukushima context. The creation of new knowledge directly benefits Japan and potentially assists other IAEA's Member States with similar situations.

Key words: Science and Technology Studies (STS); Nuclear Accident; Fukushima; International Atomic Energy Agency; Human Health

[PROFILE] Rethy K. Chhem (Director, Division of Human Health, IAEA)

Dr. Chhem was born in Cambodia. He holds a medical degree from the University of Paris VI, a PhD in education and a PhD in history, both from the University of Montreal. For the last 20 years, he taught radiology at the University of Sherbrooke, McGill University, and University of Western Ontario in Canada and at the National University of Singapore. His history thesis was on medicine and public health in 13th century in the Khmer empire at Angkor. He was the former Chair of radiology and nuclear medicine at the University of Western Ontario. He is currently the director of the Division of Human Health at the International Atomic Energy Agency and is a guest professor at the Medical University of Vienna and Ulm University. He has published 9 books with one on Paleoradiology of mummies and fossils. His current research encompasses the history and philosophy of medicine and science with a focus on medical imaging, paleoradiology, Angkorian medicine and natural history in Southeast Asia. For more curriculum vitae, check the following website:

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(11\)60082-2/](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60082-2/)

Lecture 1

Rehabilitating Living Conditions after a Nuclear Accident: Lessons from Experience

Jacques Lochard

Nuclear Protection Evaluation Centre (CEPN)
Fontenay-aux-Roses, France



The sudden irruption of radioactivity in the close environment of a population, whether resulting from accidents or malevolent events or discoveries of consequences from past activities, is creating a new reality which is altering all aspects of individuals' living conditions of those affected: psychological, health, social, economic and cultural. The experience in the contaminated territories by the Chernobyl catastrophe in Europe has revealed that the daily confrontation with such situation over years is progressively creating a general feeling of loss of control and insecurity which is difficult to solve by just introducing radiological norms and countermeasures. The prescriptive and normative traditional modes of administrative management are unable to properly address the complexity of the problems resulting from the contamination. The radiological protection dimension tends to become dominant in the daily choices concerning the living conditions of the inhabitants. Failing to be integrated into a qualitative approach of protection grounded on a shared knowledge of the radiological situation and its consequences, the prescriptions and norms gradually alienates these living conditions without the possibility to rebuild safe and responsible new ones.

How to reduce the complexity characterizing a post-accident situation? How to avoid perverse mechanisms introducing distrust, loss of confidence and the de-mobilization of the population? These are the main challenges associated with the long-term rehabilitation of living conditions in contaminated territories. The Chernobyl experience has demonstrated the necessity and also the feasibility of the direct involvement of the inhabitants, the local authorities and the local professionals in the long-term rehabilitation process to overcome the difficulties generated by the presence of the contamination. However shifting from a centralized, top-down, prescriptive and normative approach to a more decentralized, bottom-up and quality driven approach is not

straightforward. In particular, there is a need to combine rehabilitation with sustainable development and to adopt an integrated approach dealing with health, economic and social development, environment, education and culture at the same time.

[PROFILE] Jacques Lochard (Director, Nuclear Protection Evaluation Centre (CEPN))

Jacques Lochard was educated in Economics at the University of Besançon-France (BS) and Paris-Panthéon-Sorbonne (MS). After 3 years experience as a teacher he joined the Centre d'étude sur l'Évaluation de la protection dans le domaine Nucléaire (CEPN) as a research associate in 1977 and became its director in 1989. CEPN is a non-profit organization, founded in 1976, for research and consulting in the nuclear energy area in the evaluation of the technical, health economic and social dimensions of radiation protection. The objective was to open the discipline to the social sciences and the emerging concepts of risk assessment and management (<http://www.cepn.asso.fr/>). His main contribution in radiation protection has been in the development of methodologies for the implementation of the optimisation principles. He has published many articles in scientific journals and in the proceedings of international conferences covering both the theoretical and practical aspects of optimisation. He has been President of the French Society of Radiation Protection (SFRP) from 1997 to 1999. He is also widely involved in the international radiation protection scene. He is the Executive Officer of the International Radiation Protection Association (IRPA) since 2000. He was the Chairman of the Committee on Radiation Protection and Public Health (CRPPH) of the OECD Nuclear Energy Agency from 2005 to 2009. He joined ICRP in 1993 as secretary of Committee 3, became a member of Committee 4 in 1997 and it's Chair in 2009. For more curriculum vitae, check the following website:

http://www.icrp.org/icrp_membership.asp

Lecture 2

Detailed investigation of radionuclides distributions caused by the Fukushima Daiichi nuclear disaster

Tokushi Shibata

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After the Fukushima Daiichi nuclear disaster, the detailed investigation of radionuclides was indispensable for health protection of population in Fukushima and also remediation and countermeasures of environment. The most concern on exposure effects on health of population is the thyroid dose due to intake of ^{131}I , because the experience of Chernobyl accident showed short term functional thyroid changes and thyroid cancer effects.

Since the half-life of ^{131}I is 8.0 days, the investigation of radionuclides distribution should be complete as soon as possible. In these circumstances researchers in the nuclear physics field had a first meeting to discuss what can be done for reconstruction supports for the disaster on March 16, 2011 at Research Center for Nuclear Physics (RCNP), Osaka University. They started the supportive action to attend the screening for the people evacuated from the high dose rate area which was conducted by the Ministry of Education, Culture, Sports, Science and Technology (MEXT). During the supportive action for screening, they recognized the importance of detailed investigation on distribution of radionuclides deposited on environment due to the disaster. The investigation requires obtaining soil samples from many points and to measure the samples by gamma-ray detectors. Since the number of samples needed to get enough information is an order of about 10,000, the required number of people attending the sample collection and groups for gamma-ray measurement are extremely large. This means that a big project involving many people and organizations is required. Thus this project is desirable to be carried out in collaboration with many universities and research facilities. To promote the project, they worked on the Science Council of Japan to issue the emergency recommendation on the necessity of the investigation of radiation levels and distributions of radionuclides from the nuclear power plant

accident. Their effort was successfully rewarded as the 2nd emergency recommendation “Regarding on the necessity of the investigation of radiation levels after the accident of the Fukushima Daiichi Nuclear Power Plant” was issued on March 25, 2011. This recommendation encourages many people in universities and research facilities.

The head of Center for Nuclear Study (CNS), the University of Tokyo also announced their participation in the supportive action on March 29, 2011. The researchers in fields of nuclear physics, radiochemistry, health physics, geoscience, marine science had a meeting at the School of Science, University of Tokyo on April 13, 2011 to discuss on the promotion of the detailed investigation on radionuclides distribution caused by the accidents.

The project on the detailed investigation on radionuclides distribution was finally approved as a project of MEXT. The details of the MEXT project are 1) the soil sample collection points are 2 km mesh points in the area of 80 km from the Fukushima Daiichi Nuclear Power plant and 10 km mesh points between 80 km to 100 km from the Nuclear Power plant and 5 samples are collected at each point, the positions of the collection points is measured by the GPS monitor, 2) the method of soil sample collection should be follow the manual described by researchers of the Tsukuba University, 3) the air dose rate at 1m above of the sample collection points is measured and 4) all the sample collected are sent to CNS then the samples are sent to the research facilities to be measured by Ge detectors. The project started on June 5 and continued to June 15 as the 1st action, and 2nd action was from June 27 to June 30. The number of people cooperated with the sample collection was 440 persons from 98 organizations of universities, research facilities, medical institutes, private companies, and etc. The 60% of samples were measured by the collaboration of 21 organizations of universities and research institutes, The 40% of samples were measured by Japan Chemical Analysis Center.

The other activity was measurement of air dose rate on the roads by the car loading a compact measuring systems (KURAMA) consisting of a survey-meter and a communication device. The system was newly developed by a group of the Kyoto University Research Reactor Institute.

The radionuclides distribution maps of ⁸⁹Sr, ⁹⁰Sr, ^{129m}Te, ^{110m}Ag, ¹³¹I, ¹³⁴Cs, ¹³⁷Cs, ²³⁸Pt, ²³⁹Pu and ²⁴⁰Pu and the maps of air dose rate were published in the home page of MEXT.

This project was an unprecedented project involving many peoples from many organizations. The successful achievement was completed by individual effort should be commended.

[PROFILE] Tokushi Shibata

(Special Appointed Researcher at J-PARC Center, Japan Atomic Energy Agency)

Dr. Shibata received his PhD at Osaka University. After working for Osaka University, he became a professor at Tokyo University. Currently, he is an emeritus professor at Tokyo University, and a special appointed researcher as well as safety adviser at J-PARC Center, Japan Atomic Energy Agency. He is specialized in Nuclear Power Science, related to Physics, Integrated engineering, and Nuclear engineering. For more curriculum vitae, check the following website :

<http://researchmap.jp/read0170735/?lang=english>

Lecture 3

Inventories of radionuclides in wetland ecosystems in Fukushima Prefecture, Japan

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The National Institute for Environmental Studies (NIES) has conducted studies with aim to contribute to understanding the long-term behavior of atmospherically-derived radionuclides deposited on the ground by emission of radiation at the time of a nuclear accident of Fukushima Daiichi Nuclear Power Station (FDNPS). Present report reviews a series of studies among them which have especially dealt with the behavior of those radionuclides in wetland ecosystems. The studies cited include investigations of the evaluation of the transport rate of the atmospherically-derived radionuclides from the ground via a river to the downstream area where the affected water is consumed. The investigations in the Utagawa, Manogawa, Niidagawa and Ohtagawa watershed with $^{134+137}\text{Cs}$ has validated 1) the importance of suspended solids (SS) in the fluvial discharge of those radionuclides, and 2) to estimate the discharge of those radionuclides based on regression analysis with the river flow rate. NIES also investigated the vertical profiles of $^{134+137}\text{Cs}$ in sediment core samples obtained from four rivers and brackish wetlands situated north direction from the FDNPS. From a viewpoint of their distribution among water, suspended solids, sediment, aquatic plants and benthic animals and fishes, the form of radionuclides released by the accident in rivers and brackish wetlands were analyzed.

There were several peaks of water level in the Utagawa, Manogawa, Niidagawa and Ohtagawa rivers because of heavy rain on the mountainous land and farmland in 2012. Those heavy rains led flooding and high concentration of suspended solids adsorbed with $^{134+137}\text{Cs}$. The maximum $^{134+137}\text{Cs}$ in suspended solids was about 20 Bq/L in Niidagawa in April 2012. The concentration of $^{134+137}\text{Cs}$ in suspended solids had two peaks to respond to flooding in 2012. The vertical profiles of $^{134+137}\text{Cs}$ in wetland sediment in four rivers had also clearly two peaks (Fig.1).

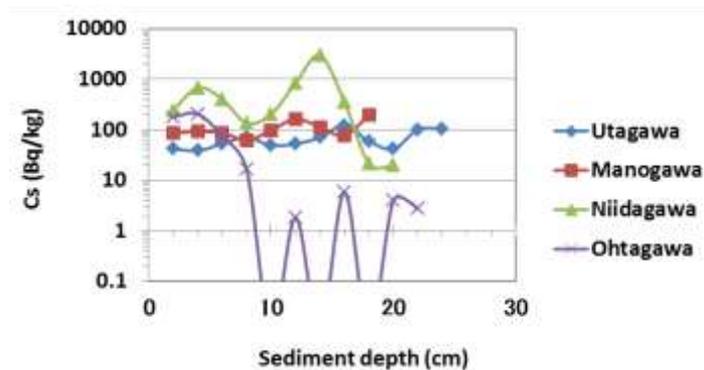


Fig.1 Vertical profiles of $^{134+137}\text{Cs}$ in wetland sediment

On the other hand, the vertical distribution of $^{134+137}\text{Cs}$ in Matsukawaura tidal flat of downstream of Utagawa River had one peak. The concentration of $^{134+137}\text{Cs}$ in tidal flat sediment in Matsukawaura tidal flat was extra-high level in muddy sediment such as closed-off section of tidal flat. Those areas were secondary hotspots of radionuclides.

The accumulation of $^{134+137}\text{Cs}$ in tidal flat sediment was decreased with distance from FDNPS. The concentration of $^{134+137}\text{Cs}$ in tidal flat sediment in Niidagawa River (6,000 Bq/wet kg) was higher than other tidal flats in March 2012. The concentration of $^{134+137}\text{Cs}$ in wetland sediment in Niidagawa River (800 Bq/wet kg) was maximum in four wetland sediments in June 2012. The concentration of $^{134+137}\text{Cs}$ of aquatic plant in wetlands in Niidagawa River (400 Bq/ dry kg) was also higher than other wetland sites in June 2012.

The accumulations of $^{134+137}\text{Cs}$ in aquatic benthic animal and fish were taken on a different posture like no other. The concentrations of $^{134+137}\text{Cs}$ of fresh fish (4,900 Bq/ wet kg), shrimp (2,700 Bq/wet kg) and crab (381 Bq/wet kg) in Ohtagawa River were higher than other rivers in April 2012. The accumulation of $^{134+137}\text{Cs}$ in aquatic benthic animals and fishes was decreased with distance from FDNPS.

These data will be useful background information to assess the concentrations in many rivers and tidal flats in Tohoku district of artificial radionuclides released from the FDNPS. The obtained findings and the methodologies in these studies will be important in quantifying environmental affections caused by a broad, radioactive contamination in wetland ecosystems of downstream environment which might become threatening in future.

[PROFILE] Seiichi Nohara

(Head of Center for Environmental Biology and Ecosystem Studies (Ecosystem Function Research Section))

Dr. Nohara's expertise lies in wetland ecology, plant ecology, analysis of stable isotopes, and environmental assessment. He has visited most of the waterfronts in Japan, including Kushiro Marsh, Akai Wetland, Ozegahara Marsh, Miomote River, Lake Kasumigaura, Hinuma Bog, Banzu Natural Tidal Flat, Ise Bay, and Ishigaki Island. He has devoted his life to the study of red snow in early spring and *Elodea nuttallii* in summer in Oze Swamp. Recently, he has been working on biodiversity research. He is also working on a survey of anthropogenic influences on ecosystem functions by extracting the unit construction of salt marshes, tidelands, and marine forests in estuaries from landscape ecological and hydrogeomorphological perspectives using airplane remote sensing, and by clarifying material circulation functions, including primary production and degradation rates, and distribution and community structures for each unit. For more curriculum vitae, check the following website:

<http://www.nies.go.jp/rsdb/vdetail-e.php?id=100147>

Lecture 4

Medical Management of Radionuclide Internal Contamination in Mass Casualty Scenarios Involving Fission Products, Such as in Nuclear Power Plant Accidents

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Some medical countermeasures are available for mitigation or aversion of the radiation dose from radiations from fission product radionuclides which have entered the body through inhalation ingestion, skin or open wounds. Such intakes of radionuclides then subsequently enter the systemic circulation and are incorporated into organs and may thereby cause stochastic (primary cancer) and even deterministic risks. In the case of a dirty bomb or a Nuclear Power Plant (NPP) accident contamination and incorporation might occur from inhaling fission products as the plume fallout descends or from the subsequent resuspension of the fallout on the ground, or from ingesting contaminated water or food contaminated. The initial challenge is to determine the type and quantity of radionuclide(s) causing the internal contamination and then to medically triage for those who should be treated and who should be treated first with the appropriate radionuclide specific medical countermeasure(s) as an attempt to mitigate the integrated dose which would occur if the individual is left untreated. Suitable drugs and procedures are currently available for the treatment of most radionuclide intakes. These countermeasures essentially work by reducing the residence times of radionuclides in the body or organ which in some cases, if untreated, could be as long as for the lifetime of the patient.

The exact spectrum of hundreds of fission products produced in a NPP accident varies somewhat depending on whether the NPP fuel is uranium or plutonium based.

But, some of the more medically significant metabolically active radionuclides distributed into the environment, following NPP accidents, are the various isotopes of iodine, cesium, strontium,

plutonium and uranium (predominately I-131, Cs-137, Cs-134, Sr-90, Pu-239 and U-238 or 235). Albert Einstein even in 1942 cautioned about the possible threat to human life from the release of radionuclides into the environment.

There are some general categories of medical countermeasure drugs. Specifically, decorporating and blocking agents may be tailored to internally contaminating radionuclide (s) of concern. In fission product producing scenarios, the use of concurrent multiple drug combinations at times may even be necessary. These countermeasures are used to avert and reduce the long term dose (the committed effective dose equivalent, CEDE) to the body from the presence of the contaminating radionuclides, which essentially work by increasing the elimination rate of the nuclide from the body into the urine, stool or by blocking its uptake, or both. Some medical countermeasure work very simply such as for the treatment of tritium, for example, where all one needs to do is drink three (3) to four (4) liters of water a day to facilitate the rate of tritium excretion.

Other drugs are more complex in their mechanism of action such as Prussian Blue (ferric ferrocyanate) which when given in oral capsules binds to cesium isotopes in the gastrointestinal tract and thereby interrupts the normal hepato-enteric cycle of Cs.

Specifically when Cs combines with the Prussian Blue in the GI tract, this Cs/PB complex becomes insoluble in the GI tract and is then eliminated via fecal excretion.

Fig 1 is an example of the efficacy of such treatment where in the Goiania Cs-137 accident many were internally contaminated; but, they were successfully treated with Prussian Blue i.e., the biological half life of the Cs-137 (and the consequent committed dose) was reduced by approximately 50%.

Goiania Data

Table 2: Cesium-137 Effective Half-life During and After Treatment with Insoluble Prussian blue (In Days, by Age, and Dose of Insoluble Prussian blue)					
Group	Age (Years)	Insoluble Prussian blue dose (grams/day)	No. of Pts.	During Insoluble Prussian blue Treatment - ¹³⁷ Cs T _{1/2}	Off Insoluble Prussian blue Treatment - ¹³⁷ Cs T _{1/2}
Adults	> 18	10	5	26 ± 6 days	80 ± 15 days (all 21 adult patients)
Adults	> 18	6	10	25 ± 15 days	
Adults	> 18	3	6	25 ± 9 days	
Adolescents	12 -14	< 10	5	30 ± 12 days	62 ± 14 days
Children	4 -9	< 3	7	24 ± 3 days	42 ± 4 days

Fig.1

Chelating drugs (such as Ca and Zn diethylenetriamine pentaacetic acid) which chemically combine in the blood stream with actinides (i.e., plutonium, americium, californium, and curium) develop a soluble complex which is excreted by the kidneys in the urine, thereby preventing deposition of the actinide in target organs (bones and liver), if the DTPA is given early enough following the intake.

Fig. 2 demonstrates the committed dose to liver, lung and bone surface, if an inhalation of Plutonium is not treated early enough with DTPA.

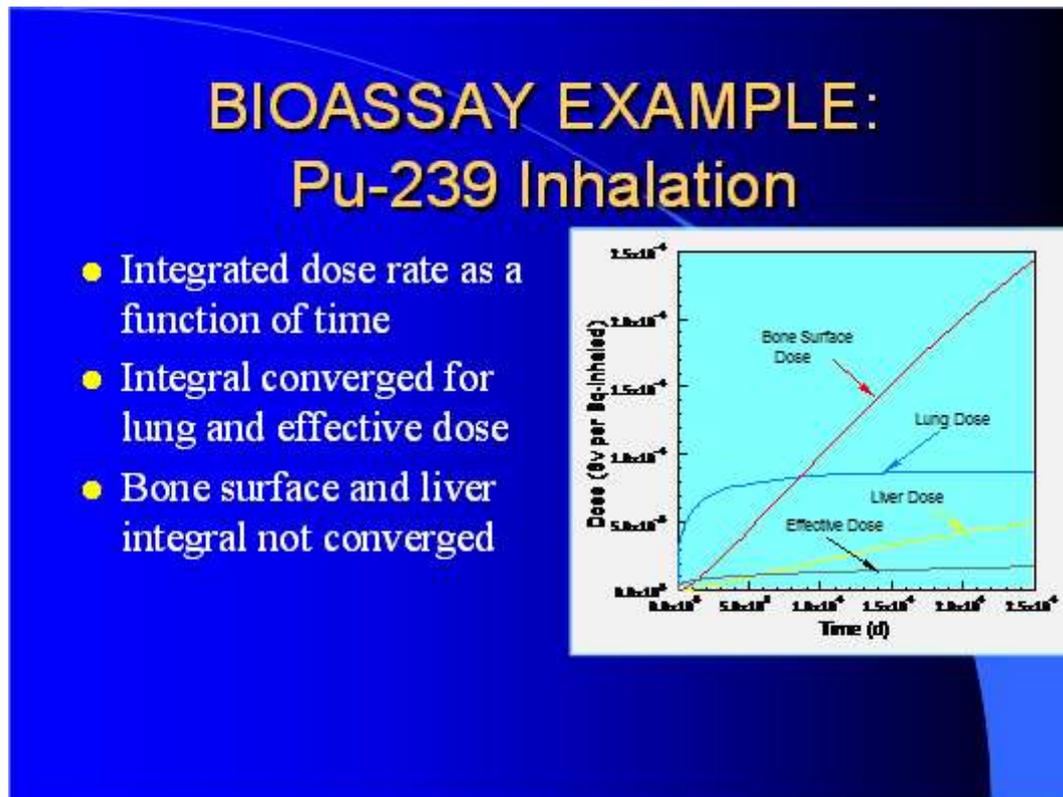


Fig. 2

Potassium iodide (KI) acts as a blocking agent by replacing uptake of the Iodine (I-131) by stable Iodine in the target organ (thyroid) during the synthesis of thyroid hormones. I-131 is a much greater risk to children under 18 years old and to the fetus than to adults. It is essential that this age group of people be treated with KI either before exposure, or within a few hours after exposure, (as was demonstrated in the Chernobyl accident where the incidence of thyroid cancer in the younger age groups was many times above the normal rate).

Radioisotopes of Strontium can be mitigated by giving calcium containing drugs (such as intravenous Ca-gluconate) where the Ca competes with or displaces Sr in the target organ (bone) metabolism. Oral administration of sodium alginate or calcium phosphate also helps to mitigate any Sr which is initially inhaled, as well as any Sr isotopes (Sr-90, Sr-89 primarily) which are ingested (primarily from milk).

Uranium can be mitigated generally by relatively simple drugs such as oral or intravenous sodium bicarbonate or some diuretics like acetazolamide. The bicarbonate ion complexes in the

blood with the uranium and forms a uranyl/bicarbonate complex which is excreted in the alkalized urine is enriched with U-235 to about 10-15%, it is not significant radiological hazard; but, it is a chemical hazard since it can cause damage to renal tubules..

Generally, metabolically active Nuclear Power Plant produced fission products are particulate (except for Iodine which is volatile) and strong beta emitters which can therefore injure the skin and eyes. Large particles (>10 microns) are generally not highly soluble chemical compounds and deposit in the upper trachea/bronchial tree and significant respiratory hazards are therefore unlikely to pose short-term deterministic effects from internal contamination by inhalation on populations. The stochastic risks to populations exposed, however, may be significant and eventually need to be addressed after the early phase emergency measures, such as shelter in place and/or evacuation, have implemented.

Accordingly, as part of the US medical preparedness for possible IND scenarios, the Strategic National Stockpile (SNS) was advised to stock KI, Prussian Blue, Ca and Zn -DTPA (Ref. 7).

The medical/public health requirements and logistics for mass casualty medical management of internal contamination with medical countermeasures are complex. The radionuclides of concern will initially need to be specifically identified; and the populations at risk will then need to be triaged with respect to who needs treatment --and, who needs it first. Additionally, the question of when to stop treatment can also be complex. (The answers to such questions are also very scenario dependent, since some countermeasures should be started earlier than others).

Special laboratories (private, DOE, CDC, EPA) need to be prepared to handle large numbers of bioassay specimens (urine, feces, etc); there will also be a need for whole body, lung and thyroid counting equipment.

A new operational quantity, CLINICAL DECISION GUIDANCE (CDG), has recently been defined and proposed as an operational tool in NCRP161 to facilitate mass casualty management of internal contamination.

The CDG is defined as the maximum, once-in –a lifetime intake of a radionuclide which represents: “Stochastic risk”, as judged by the calculated Effective Dose (ED) over 50 years for intake by adults (and to age 70 by children) that is in the range of risks associated with guidance on dose limits for emergency situations (DOE, 2008, FEMA, 2008, ICRP, 1991, NCRP, 2005) and, based on these recommendations, the numerical values in tables are developed for 30 radionuclides (excluding Iodine isotopes). The basis for computing the CDG values for these 30 different radionuclides in adults are dose thresholds of 0.25 Sv (25 rem) for consideration of stochastic risks –and, a 30day RBE –weighted absorbed –dose value of .25 Gy (25 rad-Eq) for consideration of deterministic effects to the lungs.

Thus, the intake for intake of a radionuclide (other than iodine) in the adult CDG is the maximum intake which satisfies these dose constraints for the causing stochastic and deterministic effects, which may be expressed as:

$$CDG = \text{MIN} \left[\frac{0.25 \text{ Sv}}{e(\text{Sv Bq}^{-1})}, \frac{0.25 \text{ Gy-Eq}}{d_{\text{Red Marrow}}(\text{Gy-Eq Bq}^{-1})}, \frac{1.0}{d_{\text{Lung}}(\text{Gy-Eq Bq}^{-1})} \right] \quad (11.1)$$

where:

e = effective dose coefficient for the radionuclide

$d_{\text{Red Marrow}}$ and d_{Lung}
= RBE-weighted absorbed-dose coefficients for red marrow and lung, respectively

MIN = minimum value of the three arguments

The CDG was developed primarily as a tool for helping treating private community physicians (most of whom are not accustomed to health physics units and terminology) to decide on whether or not to treat an internally contaminated person with dose averting drugs, through the use of the simple CDG tables in NCRP161, which correlate increasing radiological risks with increasing CDG values, as obtained from routine clinical bioassays, such as the patient's urine activity (routinely reported in Bq).

In summary, internal contamination treatment with medical countermeasures is not the immediate, high medical priority following a mass casualty fission product contamination scenario since trauma, burns, etc. are the more important immediate, life- saving concerns. Appropriate early sheltering and or evacuation, as well as embargo of contaminated water /milk/food, provides the best preventive medicine for protection from internal contamination.

The main deterministic risk in such fission product scenarios is primarily limited to the neo-natal thyroid and the thyroid of children <18yo. There will, however, be long term, medically serious stochastic risks from internal contamination; and, this will require the treatment of many people by many physicians who are not trained to use radiation medical countermeasures (ie., dose averting drugs); and this will also require the "just in time" education of many private community physicians on the use of these drugs, including teaching them how to use the CDG tool.

Finally, further estimation of combined external and internal dose and consequent stochastic risk to the general population, in such mass casualty scenarios, dicentric and micronuclei biodosimetry of peripheral lymphocytes may be useful and will also be discussed.

General References

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[PROFILE] Albert Lee Wiley (Technical Director, REAC/TS)

Albert L. Wiley, Jr., BNE, MD, PhD is the Medical and Technical Director at REAC/TS and Head, WHO Collaborating Center at Oak Ridge. His professional career began as a Nuclear Engineer with a Bachelor of Nuclear Engineering and an AEC (ORINS) sponsored fellowship for nuclear engineering graduate studies at North Carolina State University. He worked in the nuclear industry prior to obtaining an MD degree from University of Rochester School of Medicine, and later a PhD in Radiological Sciences (radiobiology) from the University of Wisconsin Graduate School of Letters & Science. He received residency training in Radiation Therapy & Nuclear Medicine at the University of Wisconsin Medical Center and at the Stanford University Medical Center in Palo Alto, Calif. He is currently Professor Emeritus at the Department of Radiology & Human Oncology at the University of Wisconsin – Madison and was, prior to coming to REAC/TS, professor and chairman of the Department of Radiation Oncology, and Cancer Center interim Director at East Carolina University, Greenville, NC. He has over 180 journal, book and abstract publications in radiation oncology, nuclear medicine, radiobiology and radiation medicine. In recent years he has served as the medical team leader on NNSA sponsored training and exercises in Iraq, Kuwait, Korea, South Africa, Morocco, Vienna (IAEA), Argentina, Israel, Mexico, Ukraine, Singapore and Japan. He is also a retired member of the USN Reserve (retired). For more curriculum vitae, check the following website;

<http://orise.orau.gov/reacts/symposium/speakers/Wiley.html>

Lecture 5

Radiobiology in the Context of Radiation Protection

During a Radiological Event

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Radiation is ubiquitous in our environment. Exposure to ionizing radiation from man-made source such as nuclear medicine and diagnostic radiology now overtakes environmental radon as the principal source of background radiation to humans. Since the devastating event of September 11th, 2011 in New York City where the World Trade Center twin towers were destroyed with the loss of more than 2,600 lives by a terrorist act, there has been increasing concern of a radiological incidence in the mind of citizens and governmental agencies around the world. As a result, emergency management programs have been set up in many countries on ways to respond to such a nuclear threat. While threat from nuclear device is remote and from power plant accidents such as Chernobyl and, more recently, from Fukushima Daiichi is rare, threat from radioactive dispersal devices is real. Fortunately, the extent of the radiation dose from these devices is likely to be small and the exposure range is limited. Nonetheless, the psychological factor and the panic response from the public are going to be huge. As such, a critical issue in risk management is a balance between overreaction and responsible measure and this is particularly true in radiation induced cancer incidence.

Radiation is a well established human carcinogen. The life time cancer mortality risk from radiation, based on epidemiological data from the Japanese atomic bomb survivors, is estimated to be 0.05 per sievert. However, direct characterization of risk at lower doses is at or beyond the limits of epidemiology. Cancer risks from exposure to ionizing radiation clearly increases at dose above 10 cGy and no obvious threshold dose is detectable. At doses below 10 cGy, a conceivable dose involving a radioactive dispersal device, the radiobiological effects are rather

complex and are subjected to modulations by various competing forces including bystander effects, adaptive response, genomic instability and genetic susceptibility of the exposed individuals. Radiation-induced bystander effects suggest that cells and tissues that are outside of the irradiation field may also contribute to the biological consequences of exposure to low doses of radiation. Although cyclooxygenase-2 and reactive radical species have been shown to be important in mediating the bystander/non-targeted response, it is likely that multiple pathways are involved and that different cell types respond differently to the bystander signalling. Furthermore, the observations that heritable DNA alterations can be propagated to cells many generations after radiation exposure and that bystander cells exhibit genomic instability in ways similar to directly hit cells indicate that the low dose radiation response is a complex interplay of various modulating factors.

On the other spectrum, adaptive response is characterized by a reduction in radiobiological response in cells pretreated with a low dose of ionizing radiation (generally $\leq 10\text{cGy}$) followed by exposure to a challenging, higher dose. There is evidence that adaptive response can mitigate the bystander response in mammalian cells. Thus, these two events appear to operate in different directions. In general, there are more similarities than differences between the two phenomena. Both are primarily low dose phenomenon and neither of them shows a dose response induction of effects. Both the adaptive response and the bystander effect have been demonstrated by a range of biological endpoints and both phenomena involve signals that mediate through either gap junctions or soluble mediators.

A better understanding of the cellular and molecular mechanisms of these low dose phenomena will allow us to formulate a more accurate model for assessing the health effects of low doses of ionizing radiation and to address the modern day radiological risk challenge using an evidence-based approach.

[PROFILE] Tom Hei (Professor and Vice-Chairman of Radiation Oncology, Columbia University Medical Center)

Dr. Tom Hei received his B.Sc. (Summa Cum Laude) from the University of Wisconsin-Whitewater and his Ph.D. in experimental pathology from Case Western Reserve University. He has been on the faculty of Columbia University since 1983 and is currently Professor of Environmental Health Sciences in the Mailman School of Public Health and Deputy Director of the NIEHS Center for Environmental Health in Northern Manhattan. Dr. Hei's primary appointment is Professor and Vice-Chairman of Research in Radiation Oncology and the Associate Director of the Center for Radiological Research in the College of Physicians and Surgeons. Dr. Hei has several adjunct professorships in both China and Japan.

Dr. Hei is internationally recognized for his expertise in the asbestos and fiber toxicology field. His asbestos research program, funded continuously by the National Institute of Environmental Health Sciences for more than 15 years, has made major contributions in our understanding of the basic molecular mechanism of how asbestos induces cancer through the induction. For more curriculum vitae, check the following his website:

<http://www.cumc.columbia.edu/dept/radoncology/crr/hei.htm>

Abstracts

Poster session

February, 11, 2013

9:00-10:20

International Conference Center

Hiroshima

Room : Dahlia 2

Identification of integrin $\beta 3$ L718P mutation in a pedigree with autosomal dominant thrombocytopenia with anisocytosis

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α IIB β 3 integrin mutations that result in the complete loss of expression of this molecule cause Glanzmann's thrombasthenia. This is usually an autosomal recessive, while other rare mutations cause dominantly inherited thrombocytopenia. Here we report a 4-generation pedigree affected by dominantly inherited thrombocytopenia. Six individuals of them carry a non-synonymous *ITGB3* gene T2231C alteration resulting in integrin $\beta 3$ -L718P.

The proband was a 4-year old girl who presented with mild bleeding tendency. Her platelet count was $49-72 \times 10^9/L$ with marked platelet anisocytosis and macrothrombocytes. Platelet aggregation was markedly reduced and the α IIB β 3 expression level was 50-60% of the healthy control. To isolate a candidate gene alteration responsible for the thrombocytopenia, whole exome sequencing analysis was performed using genomic DNA obtained from four affected individuals of the pedigree. Among the 90 non-synonymous alterations commonly found in the affected individuals, we focused on the heterozygous integrin $\beta 3$ -L718P mutation.

Resting platelets from affected individuals showed a mild but significant increase of a ligand-mimicking PAC-1 binding relative to healthy individuals. However, in ADP-treated platelets carrying the mutation, only a small increase of affinity to PAC-1 was observed. These findings suggest that α IIB β 3-L718P is partially activated in the absence of inside-out signals such as ADP, but nevertheless cannot be fully activated in the presence of stimulating signals. This was confirmed by an experiment using CHO cells expressing α IIB β 3-L718P.

In summary, identification of a pedigree showing autosomal dominant inheritance leads to a model whereby the integrin $\beta 3$ -L718P mutation contributes to thrombocytopenia most likely through gain-of-function mechanisms.

Analysis of binding site of ubiquitin ligase, human double minute 2 in integrin $\beta 8$ in Oral Squamous Cell Carcinoma cell lines

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[Introduction]

We have shown that integrin $\beta 8$ was ubiquitinated by human double minute 2 (Hdm2), E3 ubiquitin ligase, and degraded by proteasome in oral squamous cell carcinoma (SCC) cells. In present study, we examined the binding site of Hdm2 in integrin $\beta 8$.

[Experimental procedures]

To detect the interaction between $\beta 8$ and Hdm2, mammalian two-hybrid assay was performed. $\beta 8$ and Hdm2 genes were subcloned into pVP16 vector, a vector for the transcriptional activation domain of VP16 and pM vector, a vector for the DNA-binding domain of the GAL4, respectively. Several deletion mutants of $\beta 8$ subcloned into pVP16 were constructed by inverse PCR. The $\beta 8$ deletion mutants, pM vector subcloned with Hdm2, and pG5SEAP reporter vector were co-transfected into A431, human vulval SCC cells. After 48 h of transfection, the secreted alkaline phosphatase (SEAP) activity in the conditioned medium was measured.

[Results and Conclusion]

The mammalian two-hybrid assay using the $\beta 8$ deletion mutants indicated that the deletion of the amino acids 481-576 of $\beta 8$ led to significant loss of interaction with Hdm2, suggesting that the binding site of Hdm2 exists in EGF-like repeat domains in integrin $\beta 8$ subunit leg.

Generation of disease-specific human induced pluripotent stem (iPS) cells from dental pulp cells of a patient with Cleidocranial dysplasia in serum- and feeder-free culture.

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BACKGROUND : The recent advances in the induced pluripotent stem (iPS) cell research have been focused on not only on regenerative medicine but also on drug discovery and developmental biology. Human iPS cells are commonly maintained on inactivated mouse embryonic fibroblast as feeder cells in medium supplemented with FBS or proprietary replacements. Use of culture media containing undefined or unknown components has limited the development of applications for pluripotent cells because of the relative lack of knowledge regarding cell responses to differentiating growth factors. In the field of genetic diseases, iPS cells have become an appealing choice for elucidate pathogenesis and treatments. In this study, we generated disease-specific iPS cells derived from dental pulp cells of a patient with Cleidocranial dysplasia (CCD). CCD is an autosomal dominant inherited skeletal disease characterized by hypoplastic or absent clavicles, increased head circumference, large fontanels, dental anomalies, and short stature, caused by mutations in *Runx2 (Cbfa1)* which shows the abnormal differentiation of bone and cartilage.

METHODS AND RESULTS : We have successfully generated disease-specific human iPS cells from dental pulp cells of a CCD patient using Yamanaka's factors (Oct3/4, Sox2, Klf4 and c-Myc) with retroviral vectors in serum- and feeder-free defined medium on fibronectin-coated culture condition. CCD-iPS cells retained the property of self-renewal and have an undifferentiated phenotype by virtue of the expression of Oct3/4, Nanog, Sox2, Esg1, Rex-1 and alkaline phosphatase (ALP). Furthermore, we found that CCD-iPS cells express several human embryonic stem cell marker proteins. It has been confirmed that CCD-iPS cells could differentiate into all three germ layers in embryoid body formation assay *in vitro* and teratoma formation *in vivo*. To identify the differentiation ability of CCD-iPS cells, we evaluated their osteogenic and chondrogenic differentiation activities. It has been revealed that ALP activity exhibited a striking impairment in osteogenic differentiation of CCD-iPS derived cells compared to that of wild-type human iPS derived cells. Difference in chondrogenic activity was further confirmed by Alcian Blue staining and proteoglycans synthesis. This impairment was further supported by real-time PCR analysis of chondrogenic marker genes such as RUNX2, collagen2A1, and collagen10A1.

CONCLUSIONS : We have developed a serum-free defined medium for establishing and culturing hiPS cells, can maintain proliferation, self-renewal and pluripotency without using feeder cells. As this simple serum-free adherent monoculture system will allow us to elucidate the cell responses to growth factors under defined conditions, and can eliminate the risk might be brought by undefined pathogens. By using this culture system, we have successfully established disease specific iPS cells from Cleidocranial dysplasia patient. Further characterization of the cells in the serum-and feeder-free culture would be beneficial to clarify the molecular mechanism involved in the disease.

Participation of heterodimer formation with integrin αv subunit in the stability of integrin $\beta 8$ subunit in squamous cell carcinoma cells

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[Introduction]

Integrins were heterodimeric transmembrane receptors for extracellular matrix (ECM) proteins, which are consisted with one α subunit and one β subunit. Formation of the α/β heterodimer is essential for the expression and the function of integrins on cell surfaces.

Our previous study has shown that the expression of integrin $\beta 8$ subunit is regulated by ubiquitin-proteasome system in some oral squamous cell carcinoma (SCC) cells. In present study, we examined the effect of the formation of α/β heterodimer on the stability of $\beta 8$ subunit in SCC cells.

[Experimental procedures]

Integrin αv gene was subcloned into mammalian expression vector pCI-neo, and the resultant plasmid was termed as pCI/neo- αv . Human vulval SCC cell line A431, which expresses little amount of mRNAs of integrin αv and $\beta 8$, was transfected with pCI/neo or pCI/neo- αv , and A431mock or A431 αv were isolated, respectively. Next A431mock and A431 αv were transfected with a tetracycline (Tet) inducible expression vector pCDNA4/TO containing $\beta 8$ gene, and A431mock/ $\beta 8$ -On and A431 αv / $\beta 8$ -On were isolated. Altered expression of $\beta 8$ protein induced by tetracycline was examined in A431mock/ $\beta 8$ -On and A431 αv / $\beta 8$ -On.

[Results]

Treatment with Tet induced the expression of $\beta 8$ protein in both A431mock/ $\beta 8$ -On and A431 αv / $\beta 8$ -On. Sequential cultivation in the absence of Tet led to a gradual decrease in the expression of $\beta 8$ protein in A431mock/ $\beta 8$ -On, and almost complete loss of $\beta 8$ protein was observed after 12h. In contrast, the cultivation without Tet has no influence on the expression of $\beta 8$ protein in A431 αv / $\beta 8$ -On.

[Conclusion]

$\beta 8$ subunits induced by Tet in A431mock/ $\beta 8$ -On might exist as a monomer because of the insufficiency of αv subunits available for forming $\alpha\beta 8$ heterodimer. In contrast, $\beta 8$ subunit induced by tetracycline in A431 αv / $\beta 8$ -On dimerizes with abundantly expressed αv subunit. The possibility should be considered that $\beta 8$ dimerized with αv is stable compare to $\beta 8$ monomer by the escape from ubiquitin-proteasome system.

The Role and Issues of the NPOs/ NGOs for the Disaster Revival

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Background

We have a serious situation caused by the radiation hazard of the first Fukushima nuclear plant accident. Until the stage at urgent relief led to revival, the NPOs/ NGOs worked to support people and society in stricken areas.

Study purpose:

Overlooking the activities by the NPOs/ NGOs, their organization system itself, resources to be utilized and the way how you worked will be examined and clarified.

Methods

(i)Analytical work of reports and documents published, (ii)Hearing survey to the NPOs/ NGOs staffs , the people, volunteer group at the stricken areas, and municipal government.

Results

The following things have been clarified:

(i)Activities in ten specific areas—utilization of the experience and professional knowledge of NPOs/NGOs, (ii)New networks created, (iii)Restoration of community, and (iv)Building of multi-cultural symbiosis society.

At the same time, some limitations should be indicated below:

(i)Lack of tough organizational system and insufficient fund, (ii) Lack of vision and tactics, (iii)Lack of solidarity and adjustment, and (iv)Lack of communication.

Conclusions

(1)The importance of capability reinforcement program and training for the human resources in the organization system should be proposed in the occasion of big disaster.

(2)The building of intense cooperative relationship between the NPOs/NGOs and national/ local governmental departments is required,

Can logging residuals be used for the conservation of small mammal communities in Malaysian tropical forest ?

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Toshihiro Yamada (Hiroshima Univ)
Toshinori Okuda (Hiroshima Univ)
Tetsuro Hosaka (Tokyo Metro. Univ)

Siti Aisah Shamsuddin (FRIM)



Background

Natural fallen trees have important ecological functions in the tropical forests. As for small mammals inhabiting Malaysian tropical forests, fallen trees play critical roles by creating their nests and feeds such as insects. However, selective logging decreased abundance of natural fallen trees in a Australian tropical forests (DeWalt et al. 2003) and Yasuda et al. (2002) found that selective logging decreased the population of fallen tree-dependent small mammals even 50 years after logging in Pasoh, Peninsular Malaysia. Some studies suggested the utilization of logging residuals for small mammal diversity (Thomas et al. 2012) or commercial utilization (Michael et al. 2002). Thus, the purpose of this study is to clarify whether logging residuals improve the diversity of small mammal community in logged forest.

Methods

Temengor Forest Reserve is located in Perak, Peninsular Malaysia. Investigation was held in Aug 2012 at Block5 in Temengor FR which was logged in 2010. We set 17 automatic cameras above each logging residual for 10 days. For the control, we set 18 cameras on the ground at least 25 m apart from logging residuals. Small mammals were identified into species or genus and counted the number of appearances per 10 days. Species richness and Shannon-Wiener index (H') were calculated per camera. Number of appearances, species richness, and diversity index (H') in two groups were compared by U-test.

Results

In total, we identified 8 species and 4 genera of small mammals. One species was excluded from the following analysis because of small number of appearances. Species richness and diversity index (H') were higher in the logging residuals group than in the control groups (species richness; $p < 0.001$, diversity index (H'); $p < 0.001$). Of 11 species and genera, 4 species and 3 genera were more frequently seen in the logging residuals group, while 1 genus was more in the control group.

Conclusion

Logging residuals increased both species richness and diversity index (H'). These results suggest that logging residuals can contribute to the conservation of small mammal community after logging. Focused on each species, species increased with logging residuals tended to be arboreal or utilize fallen trees as nest. This may show that logging residuals also have the same ecological functions as fallen trees. These results will help to create the developed forest management methods.

Effects of logging operation on soil CO₂ efflux in a tropical rainforest

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Background: Materials cycle in forest ecosystems affects the environment which relates to our life, and at the same time, the cycle is affected by artifactual disturbance such as forest logging and environmental pollution by radiation...etc. Therefore, evaluating the effects is very important not only for understanding of materials cycle in forest ecosystems but also for our life.

We evaluated effects of logging operation on soil respiration which is CO₂ efflux from soil surface derived from root and heterotrophic respiration in a tropical rainforest. In this study, logging operation and carbon cycle were considered as artifactual disturbance and a component which is expected to be affected by the disturbance, respectably. We divided the effects of logging operation into two categories: 1) logging roads construction and 2) selective logging inside forests.

Methods: The study site is located in Block 5, of the Perak Integrated Timber Complex (PITC) Concession Forest in the Temengor Forest Reserve, Perak, Peninsular Malaysia.

1) We established 35 m transects from the logging road into the forest and measured soil respiration at 6 points on each transect. In total, 25 transects were located within the study site. 2) We established a 20 × 100 m plot inside the forest and measured soil respiration two months before, five and eight months after the logging operation.

Results and discussion

1) Logging roads construction

Values of soil respiration rate on logging road was significantly lower than those in forest (Kruskal-Wallis test, $p = 0.0322$). This may be because the trees and the surface soil layer were removed when the logging road was constructed.

2) Selective logging inside forests

The soil respiration rate after the logging operation was 19 % lower than that before the logging operation (Friedman test, $p < 0.001$). This reduction in soil respiration rate may be due to the immediate reduction of litter fall amount occurred fluctuation subsequently after the extraction of big canopy trees.

Conclusion

The carbon cycle was surely affected by logging operation although it was not very big change and it should not be ignored.

Effects of constructing logging roads on dung beetle communities in lower mountain rain forest, Peninsular Malaysia

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Introduction

Selective logging is a mainstream logging method in tropical forests. Ecological effects of selective logging in the tropics result from logging roads, skidders, and decks. However, few studies have examined the effects of logging roads. Dung beetles provide for their young by burying feces in the soil with their eggs. This process drives ecological processes such as secondary seed dispersal and soil improvement by increasing soil nitrification. Dung beetles have important role in the forest ecosystem. And dung beetles are sensitive to change of a forest. Thus we investigated effects of roads on dung beetle communities.

Study site & Methods

Field work was conducted in Temengor forest reserve, Perak, Peninsular Malaysia. We set 95 pitfall traps with rain shields, baited with human feces (50 cc). We set 15 traps in decks (“M”), 15 traps in logging roads (“L”), 15 traps in skidders (“S”), 10 traps at 10 m from decks or logging roads in forests (“10L”), 10 traps at 10 m from skidders (“10S”), 10 traps at 30 m from decks or logging roads (“30L”), 10 traps at 30 m from skidders (“30S”), 10 traps at 60 m from decks, logging roads or skidders (“60”) in August 2012. Dung beetles were collected at 24 h intervals for two days.

Results

A total of 1286 individuals, belonging to 39 species in 11 genera and two families (Hybosoridae and Scarabaeidae) were collected. The number of dung beetles and species richness in the forest (30L, 10S, 30S, 60) is significantly larger those than in roads and decks (M, L and S). The points of 10L was inside the forests but the number of dung beetle and species richness did not show significant difference with those M, L and S.

Conclusion

We understood that 10 m from logging roads to forest sites (10L) affected the number of dung beetles and species richness. The percentage of logging roads are 3% in Block5, but if skidder, and areas of 10 m from logging roads are included , it will become about 14%. Selective logging occurred not only deforestation and forest degradation by logged forests, but also affect forest ecosystem by constructed roads. When logging operations are conducted, not only logged intensity but also roads density showed be considered.

Comparison of detection characteristics of γ - and X-ray detectors for the measurement of environmental radioactivity and identification of ^{129}Te .

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Introduction

In the case of radiation disaster such as the accident of Fukushima Daiichi Nuclear Power Plant, rapid radiation dose measurement and identification of radionuclides in the environment are necessary for public safety. Gamma-ray spectrometer with a Ge semiconductor detector in low-background shielding is a typical device for the radionuclide identification but liquid nitrogen is necessary for cooling. Thus, portable scintillation detectors are normally used for in-situ measurement. The purpose of this study is to examine portable detectors for the in-situ measurement of radioactivity in the environment.

Experimental

Two scintillators NaI(Tl)($\phi 51 \times 51 \text{ mm}$), CsI($10 \times 10 \times 10 \text{ mm}$) and two semiconductor detectors CZT($3 \times 3 \times 2 \text{ mm}$) and Si-PIN($5 \text{ mm}^2 \times 0.5 \text{ mm}$) are tested concerning to the energy resolution, detection efficiency and availability for measuring X, and γ -ray energy regions. In addition, these detectors are applied to measure contaminated soil sample obtained from Iitate Village in Fukushima Prefecture..

Results and Discussion

Obtained results are summarized as follows;

- 1) γ -ray energy region (50 keV-3 MeV): CsI(Tl) detector has better energy resolution of 6.7% than 11.4%. of NaI(Tl). The efficiency of present NaI(Tl) is 4.71% which is better than 0.1163% of CsI(Tl),.
- 2) X-ray energy region (10-80 keV): Si-PIN detector has better energy resolution of 0.69% than 1.87% of CZT. The detection efficiency of CZT is 0.085% which is better than 0.00483% of Si-PIN's,
- 3) Radionuclide measurement of Fukushima soil sample: ^{134}Cs and ^{137}Cs are identified both CsI(Tl) and NaI(Tl) detectors. Peak separation is much better for former detector. Characteristic K-X-rays of Ba coming from decays of ^{134}Cs and ^{137}Cs are observed with both CZT and Si-PIN detectors. In addition, K-X-rays of Te are clearly observed. This result indicates the existence of $^{129\text{m}}\text{Te}$ (half-life 33.5d). which has much higher internal conversion rate in its decay process.

Conclusion

It is necessary to measure not only γ -rays but X-rays for the radionuclide identification. CsI(Tl) scintillator and CZT semiconductor are profit for the measurement of γ -rays but X-rays , respectively. The radionuclide $^{129\text{m}}\text{Te}$ released from the Fukushima reactor accident can be effectively detectable in the X-ray measurement.

Nondestructive image analysis of ancient oriental bronze swords by means of gamma-ray radiography

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Introduction

Gamma-ray radiography is a method to obtain transmission images of an object by using intense irradiation source and two-dimensional image sensor such as imaging plate. This technique is especially important for nondestructive analysis of cultural properties. The purpose of this work is to investigate the internal structures and existence of defects induced during production procedure for three ancient oriental bronze swords (owned by Faculty of Letters of Hiroshima University) through the non-destructive gamma-ray radiography.

Experimental

Transmission images were obtained for 10-min irradiation from the source using an imaging plate and ^{137}Cs gamma-ray irradiation source (0.61 TBq) equipped at Research Institute for Radiation Biology and Medicine (RIRBM), Hiroshima University. In addition, we have developed a scanning radiography device to obtain transmission images of the swords using the high-intensity ^{60}Co irradiation source (50.6 TB) of Faculty of Engineering.

Results and Discussion

Transmission images were successfully obtained using ^{137}Cs gamma-ray irradiation source. A newly developed scanning radiography using intense ^{60}Co irradiation source were able to obtain transmission images with same quality from three-minutes irradiation and scanning. It was found that ancient bronze swords have iron cores in the grip of swords. Moreover, many coagulation defects were observed in the grip part of the swords reflecting the production procedure of casting method.

Conclusion

Gamma-ray irradiation source of ^{137}Cs at RIRBM can be applicable for the nondestructive analysis of thick metal samples having a few cm thickness. A scanning radiography using intense ^{60}Co irradiation source has been developed at Graduate School of Engineering. Transmission images of three kinds of ancient bronze swords revealed the existence of iron cores in the grip and many coagulation defects. Gamma-ray radiography is one of useful techniques for nondestructive analysis of cultural properties.

Differential expression and identification of novel genes in scirrhous type gastric cancer, by CAST method

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Gastric cancer (GC) is one of the most common malignancies worldwide. Among histological subtypes, scirrhous type GC is highly aggressive and has a worse prognosis because of its diffuse infiltration pattern. *Escherichia coli* ampicillin secretion trap (CAST) method is a powerful technique to identify novel genes that encode secreted or transmembrane proteins. The gene expression profiles were analyzed in scirrhous GC cell line HSC-44PE and highly metastatic cell line 44As3 derived from HSC-44PE. Among the candidate genes, ZDHHC14 (zinc finger, DHHC-type containing 14) showed higher expression in 44As3 than in HSC-44PE. Indirect immunofluorescence microscopic analysis revealed that ZDHHC14 expression was more frequently observed in 44As3 than in HSC-44PE. High level of ZDHHC14 expression was observed in 27% of GC samples by qRT-PCR. Cell invasion assay and MTT assay revealed that ZDHHC14 affected invasion and growth capacity of GC cells, respectively. These results indicate that ZDHHC14 is probably involved in invasion and growth capacity of GC cells. ZDHHC14 might contribute in the process of peritoneal dissemination of the gastric cancer cells and is a potential therapeutic target for scirrhous type GC.

The utility of miR-143/miR-145 cluster as a potential marker for radiation-associated gastric cancer

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To elucidate the mechanism and improvement in diagnosis, treatment and prevention of radiation-related gastric cancer (GC), molecular analysis of GC among atomic-bomb survivors is important. In the present study, we analyzed expression profile of microRNAs in GCs among atomic-bomb survivors by microRNA microarray and identified miR-143/miR-145 cluster with higher expression in GCs from exposed cases in comparison with those from non-exposed cases. We investigated whether miR-143/145 is useful as potential marker of radiation-associated GC. Quantitative RT-PCR analysis confirmed that levels of miR-143 and miR-145 were significantly higher in exposed GC cases than in non-exposed GC cases. We also investigated function of miR-143/miR-145 cluster in GC. These miRNAs are expressed at higher levels in normal fibroblast or cancer-associated fibroblast cell lines than in GC cell lines, indicating that major source of miR-143/miR-145 in cancer tissues is derived from stromal fibroblast rather than cancer cells. Furthermore, miR-143 and miR-145 knock down repressed collagen type III and α -SMA expression, respectively, in fibroblast cell lines. These data suggest that miR-143/miR-145 may be a marker of radiation-associated GC.

Study on hepatitis viral infection among school students in Cambodia

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[Aim]

We investigated the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) among school students in Cambodia.

[Method]

Sero-epidemiological survey was performed in Sasar Sdam Elementary School in Siem Reap province, Cambodia, in Feb. 2011 and Feb. 2012 among the 3rd grade students. With written consent from parents, questionnaire survey and hepatitis screening were done. Hepatitis viral markers, quantity of HBV DNA and HCV RNA, and genotyping were tested. This study is approved by the ethical committee of Hiroshima University and that of Ministry of Health in Cambodia.

[Results]

Total number was 162 for questionnaire (74 males and 88 females), and 159 for hepatitis screening (73 males and 86 females). Age distributed from 7 to 14 (average age: 9.1 ± 1.1 y.o). HBsAg positive cases were 5 (3.1%, 95% CI: 0.4-5.9%). They were all positive for HBV DNA, genotype C. Anti-HBc was positive in 24 cases (15.1%, 95% CI: 9.6-20.7%) and anti-HBs was positive in 23 cases (14.5%, 95% CI: 9.0-19.9%). Only one case (0.6%, 95% CI: 0.0-1.9%) was positive for anti-HCV, but HCV RNA was not detected.

[Conclusion]

Prevalence of HBV carrier was 3.1%, and 76.7% of students were neither HBV carrier nor previous HBV infected. Strategy for HBV infection is urgent problem even though universal vaccination was introduced.

What collaborative work will be useful to support aged people's health?

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Background

Health condition of aged people is very likely to go deterioration in stricken areas.

Study Purpose

The aim of this study is to propose schemes to provide aged people's health care in stricken areas through the analyses of collaborative issues among stakeholders.

Method

In this study a collaborative model for supporting aged people's health will be built referring to 55 cases reported at the Japan Society of Public Health 2011. Actual processes of disability prevention project in Hiroshima Prefecture are analyzed using this model. The study areas are Shobara city and Osaki-kamijima town. The constitution ratio of elderly people is rather high in these two areas, but there are rather few medical doctors.

Results

These actual process was divided into three stages, that is agenda-making , planning and execution stages. The stakeholders for collaboration are administrative organizations, citizens, private sectors and research institutes. As a result of analysis, various findings are clarified depending on issues for collaboration and process stages.

Conclusions

The results above mean that standardization and stiffness of projects should be avoided through collaborative work among stakeholders. This finding would supporting the health care in stricken areas.

The safety of radiation therapy for atomic bomb survivors with breast cancer.

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**Purpose/Objective**

Currently, atomic bomb survivors (ABS) who suffered from breast cancer are treated as same as usual cancer patients. However, it remains unclear whether the adverse events (AE) of radiation therapy (RT) are increased or not. The aim of this study is to clarify the safety of RT for breast cancer patients who are ABS.

Materials/Methods

We retrospectively investigated medical records of patients who received postoperative RT for breast cancer at Hiroshima University Hospital from 2005 to 2010. We selected the ABS who were officially certified by the Japanese government. Thirty-four ABS (median age 67) were recruited in this study. Median age at the time receiving ionizing radiation by atomic bomb was 4.5 years old.

Results

All patients completed planned RT and received standard dose. Median dose was 50 Gy. Median observation time was 53 months. Thirty patients were alive and 4 were dead. No patients died of AE. In acute toxicity, Grade 3 or above AE were not identified. A one patient was detected late toxicity, Grade 3 Radiation pneumonitis. Four patients developed other malignancies during follow-up.

Conclusion

Notable incensements of AE were not observed during and after RT for ABS with breast cancer. Standard dose can be administered safely to ABS with breast cancer.

Generation of induced pluripotent stem cells from dental pulp cells in serum-free and feeder-free culture condition.

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BACKGROUND : Human Embryonic Stem (hES) cells and human induced Pluripotent Stem (hiPS) cells are commonly maintained on inactivated mouse embryonic fibroblast feeders (MEF) in fetal bovine serum- or KSR-supplemented medium. However, one of the major obstacles to such uses for hiPS cells is the risk of contamination from undefined pathogens in conventional culture conditions that use serum replacement and MEF. Furthermore there is no consensus as to the optimal formulation, or the nature of the cytokine requirements of hiPS cells to promote their self-renewal and inhibit their differentiation. Previously, we have developed a growth factor-defined serum-free medium designated hESF9, for the culture of human ES cells. This medium permits their prolonged culture in an undifferentiated state without feeder cells.

OBJECTIVE : This study aims to generate hiPS cells from dental pulp cells in serum-free and feeder-free defined culture condition to elucidate the nature of the cytokine requirements of the cells to promote their self-renewal and inhibit their differentiation.

METHODS AND RESULTS : We first tried to generate hiPS cells from TIG-3 (human lung fetus origin fibroblast) cells with four factors: Oct3/4, Sox2, KLF-4, and c-Myc in hESF9 serum-free medium. Eighteen days after transduction, the hES-like cells formed flat colonies, exhibited morphology similar to that of human ES cells, and characterized by large nuclei and scant cytoplasm on fibronectin (FN)-coated dish in hESF9 medium. We next examined the generation of hiPS cells from dental pulp cells on FN-coated dish in serum-free hESF9 medium. After 18 days, the colonies with hES-like cells were observed. We picked the colonies up and continued cultivating in hESF9 on FN-coated dishes. These colonies possessed ES cell-like morphology, proliferation activities, hES cell-specific surface antigens such as Oct3/4, Nanog, Tra-1-61 and Tra-1-80, and expressed undifferentiated ES cell-marker genes such as Oct3/4, Sox2, Nanog, ESG1, Rex1 and DPPA2. Furthermore, it has been confirmed that these cells could differentiate into cell types of the three germ layers by virtue of embryoid body formation in vitro and teratoma formation assay in vivo.

CONCLUSIONS : We have successfully generated hiPS from adult human dental pulp cells and maintained in an undifferentiated state in serum-free defined medium. As this simple serum-free adherent monoculture system will allow us to elucidate the cell responses to growth factors under defined conditions, and can eliminate the risk might be brought by undefined pathogens.

The sero-epidemiological study on hepatitis viral infections
among adults in Cambodia

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[Aim]

We investigated the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) among general population in Cambodia, where hepatitis viral infections might remain an important health problem. Based on the results, We aimed to consider the prevention strategy in cooperation with Ministry of Health in Cambodia.

[Methods]

Sero-epidemiological study was performed 4 times among adults over the age of 18 in Siem Reap Province, Cambodia from Feb. 2010 to Aug. 2012, consisting of questionnaire about health and life and serologic test for determining HBV and HCV infections after obtaining informed consents. This study approved by the ethical committee of Hiroshima University and that of Ministry of Health in Cambodia.

[Results]

Total subjects were 485 adults, including 194 males and 291 females. Average age was 40.7 ± 14.7 years as of 2012. 62.5% of subjects did not feel healthy. Almost every female had pierced holes (99.0%).

Prevalence of HBs Ag, anti-HBs, anti-HBc, anti-HCV and HCV RNA were 4.6% (95%CI: 2.7-6.4, 22/483), 30.2% (95%CI: 26.1-34.3, 146/483), 38.5% (95%CI: 34.2-42.8, 186/483) 5.8% (95%CI: 3.7-7.9, 28/483) and 2.3% (95%CI: 0.95-3.6, 11/483), respectively.

[Conclusion]

In this study, the prevalence of HBV carriers and that of HCV carriers among adults in Cambodia were higher than that of same age groups in Japan.

How *Rattus spp.* select habitat in an oil palm plantation in peninsular Malaysia?

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Toshinori Okuda (Hiroshima Univ.)
Toshihiro Yamada (Hiroshima Univ.)

Noor Azlin, Y (FRIM)



[Background] In Malaysia, developing oil palm plantation is rapidly increasing from 1960s (FAO, 2009), and methods to control pests *Rattus spp.* which eats oil palms and decreases productivity of oil palm has been discussed. We need to understand ecology of *Rattus spp.* to clarify the method to control them.

[Objectives] 1. To estimate which element *Rattus spp.* actively select and escape from.
2. To clarify the method to control *Rattus spp.* inhabiting in oil palm plantation.

[Methods&Materials] The oil palm plantation we researched exists in the 500m distance south of Pasoh forest reserved in Negri Sembilan state in peninsular Malaysia (N02°57'06.3, E102°15'29.8). In the oil palm plantation, FRIM, JICA, and NIES together with local people created riverine forest in 2003 to improve the biodiversity in monotonous ecosystem by planting 351 trees which consist of 9 tree species including fruit tree species along Petekah river. In this research, we focused on 3 elements affecting emergency frequency of *Rattus spp.* Above are ground cover (which means oil palm frond and understory), the riparian planting and river. We clarified which elements affect emergency frequency of *Rattus spp.* by using tunnel tracking method which tells us whether they come to the trap in one night. We set 60 trappings for 9 days twice on August and September in 2012. We regarded the number of days in which targets left footprint out of 9 days as emergency frequency in each trap. And then, we analyzed the data by using two-way ANOVA.

[Results] 1. Ground cover effect Their emergency frequency in the ground cover is significantly higher than that in no, so it is indicated that they make use of ground cover as habitat. It is thought that removing ground covers in oil palm plantation is effective to control *Rattus spp.*

2. Riparian planting effect It is expected that riparian planting attract raptors, and they hunt *Rattus spp.* by using the trees as perch at first. But as a result the effect of riparian planting like above was not detected. One of the reasons is that raptors could use oil palms as perch which is around riparian planting, and so they don't need to use riparian planting.

3. River effect There are many insects as food resource for *Rattus spp.* around rivers in oil palm plantation. So we had expected that rivers attracted and effected them. But as a result, the effect was not detected. We considered that the effect which river has on them is not significant.

[Conclusion] There are various predators for *Rattus spp.* in oil palm plantation such as leopard cat, civet and water monitor lizard, snake. Furthermore there are no obstruction in oil palm plantation. Therefore *Rattus spp.* make use of ground cover to escape from them.

The effect of radiation to peripheral nerve in a rat model

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Introduction

The purpose of our study is to develop the animal model of partial nerve injury caused by radiation.

Materials and methods

Total of 20 Lewis rats were used for this study. We delivered radiation directly to exposed rat sciatic nerve insulating all of surrounding tissues. Rats were divided into 2 groups; 90 Gy radiated group (group R) and sham group (S group) and analyzed by walking track analysis, electromyography using muscle potential evoked by electrical stimulation of sciatic nerve and histology using toluidine blue staining.

Results

There were no statistical differences between R group and S group in the assessment of walking track analysis. Electromyography showed that the amplitude of R group was lower than that of S group. Histological assessment using axon packing density, an index for expressing “the ratio of axonal area within transversed fascicular area,” was decreased in R group compared to S group.

Conclusion

In electrophysiological and histological findings, the sciatic nerve was clearly injured by radiation. We think that the result of our study would contribute to the elucidation of mechanism or the development of novel treatment for intractable radiation induced peripheral neuropathy.

Initial assessment of the use of satellite imageries to support patrol monitoring in Mount Halimun-Salak National Park, West Java, Indonesia

Wim Ikbal Nursal

Hiroshima University, Graduate School of Integrated Arts and Sciences



Abstract

Since 2007, regular patrol along with field data collection has been conducted on Mount Halimun-Salak National Park (West Java, Indonesia). There are many themes of the data has been collected, in which some of them will be very useful for management, such as species sightings and habitat disturbances. The survey system is potential to evolve and become a model for Indonesian conservation area since the park has a good system and protocol for managing field data. In this study, the agreement of patrol monitoring data collected in 2007 with deforestation map of the park 2006 – 2007 was studied. Deforested map was produced through Image Change Detection technique by using Landsat5 Thematic Mapper 2006 and 2007 coverage. Quickbird image acquired in 2006 over the park were used for validating forest map of Landsat TM 2006. We took benefit from the archive of very high-resolution image available in Google Earth (year 2007) to justify forest cover change and validate deforestation map. We identified that encroachment data from patrol monitoring were mostly matched with changed features on deforestation map (18.4%, $n = 87$). Small level of agreement of survey data to satellite image analysis is partly because of misidentifying deforestation which influenced by the extreme topographic and climatic nature of the park. This assessment suggests that the use of satellite imageries particularly medium resolution images are remain difficult to be used for Halimun-Salak National Park management.

Geminin, an essential factor for sustaining hematopoietic stem cell activity, regulates E2F-mediated transcriptional activation

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Hematopoietic stem cell (HSC) transplantation is pivotal for treating patients with acute radiation injury as well as for treating those with late-onset radiation injury including hematopoietic malignancies. The molecular basis sustaining HSCs, however, still remains elusive. We previously demonstrated that the cell intrinsic factors sustaining the HSC activity, Hoxb4/Hoxa9 and Polycomb-group complex 1, act as independent E3 ubiquitin ligases for Geminin, suggesting that Geminin acts as a central factor for regulating HSCs. Geminin controls cellular proliferation and differentiation through the direct regulation of DNA replication licensing and chromatin remodeling. Interestingly, we found that degradation of Geminin induces transcription of a series of genes, which are under the regulation of E2Fs, including the Geminin gene. In this study we confirmed that Geminin exerts negative effect on E2F-mediated transcriptional activation by using a luciferase reporter vector with E2F-binding sequences. Curiously neither direct binding of Geminin with E2F1 or Rb nor that to the E2F-binding DNA region was, however, detected. Epigenetic histone modifications were, instead, compatible with the transcriptional induction and repression by Geminin. These findings suggest that Geminin affects the E2F-mediated transcriptional induction through the regulation of epigenetic modifications of the chromatin. We here discuss the role for Geminin in HSC regulation.

Diffusion of Radioactive Cesium into the Deeper Soil of Fukushima Prefecture

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Radioactive cesium fell on the ground surface of Fukushima Prefecture due to the discharge of the radioactive material in the accident of Fukushima Daiichi Nuclear Power Plant. This radioactive cesium causes external and internal exposures. It is important to decontaminate the radioactive cesium from living space. There are several types of decontamination. Among them, an extraction of radioactive cesium from soil becomes very important when we reuse the soil. Before we start a study of decontamination by chemical treatment, it is important to know the present situation of Fukushima soil. In the present study, we investigated the depth profile of radioactive cesium in Fukushima soil.

Soils were collected in Date City, Fukushima Prefecture on October 10th, 2012. Sampling points were 1) Under the tree by the truck farm and 2) Under outlet of the drainspout. The soils were collected in the depth of 30 cm from the ground surface. The depth profile of radioactive cesium for the collected cylindrical soils was visualized by using imaging analysis. After the acquisition of image, the collected cylindrical soils were cut by every 1 cm. The radioactivity of every portion was measured using HPGe semiconductor detector.

Imaging analysis revealed the depth profile of radioactivity. There were two types of image, spot type and spread type. The gray value decreased exponentially from the surface to the deeper soil. This reveals a diffusion process of radioactive cesium from surface to deeper position. From the depth profile, we estimated diffusion constant. Although there is minor difference between 1) and 2), the diffusion constants for both soils are in the order of $10^{-10} - 10^{-11} \text{ m}^2 \text{ s}^{-1}$.

The measurement using HPGe semiconductor detector revealed the existence of ^{134}Cs and ^{137}Cs in the soils. Both ^{134}Cs and ^{137}Cs showed a similar distribution in the soils, i.e., the radioactivity for both ^{134}Cs and ^{137}Cs decreased exponentially from the surface to the deeper soil. The change in radioactivity is similar to the results of imaging analysis.

In conclusion, it was shown that the radioactive cesium diffuses into deeper soils, although it is said that the radioactive cesium remains at the ground surface.

Relation between Environmental Radioactivity and Chemical Circumstances
in Higashi-Hiroshima Campus, Hiroshima University

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We have studied environmental radioactivity of the water sample in Higashi-Hiroshima Campus, Hiroshima University to confirm that radiation facilities in this campus do not emit radioactive materials into the environment. In the course of the study, we observed an interesting seasonal change of the environmental radioactivity in the sewage sample. It was suggested that the coexisting chemical substances or microorganisms affect the change of environmental radioactivity. On the other hand, brownish yellow microbial mats are growing at the pond and river in Higashi-Hiroshima Campus, Hiroshima University. The microbial mats capture iron hydroxides produced through biomineralization. In the present study, we investigated the relation between environmental radioactivity and chemical substances in the water samples of Higashi-Hiroshima Campus, Hiroshima University.

Water samples were collected every month from the river in Higashi-Hiroshima Campus. One is collected at 1) upper stream of the microbial mat and the other is at 2) lower reaches of the mat. For the comparison, 3) the water far from microbial mat is also collected. We measured total β -activity, γ -rays, and metal concentrations, using 2π gas-flow counter, HPGe detector, and ICP-OES, respectively.

The concentrations of Fe and Mn in samples 1) and 2) are relatively high in winter, while the concentrations are relatively low in summer. That is, the concentrations decrease with increasing water temperature, and increase with decreasing temperature. On the other hand, the concentrations of Fe and Mn in sample 3) are very low every month. The results suggest that microbial mats become active in summer and absorb more Fe and Mn in summer. Total β -activity showed an opposite temperature dependence with Fe and Mn concentrations, i.e., the activity increased with increasing water temperature and decreased with decreasing water temperature for all samples. The results suggest that the water temperature affects the total β -activity but we could not find an evidence of the effect of microbial activity on the total β -activity.

In conclusion, we found that the water temperature affects the concentrations of Fe and Mn maybe because of microbial activity. The water temperature also affected the total β -activity, but the microbial activity did not significantly contribute to the total β -activity.

Measurement of secondary neutron energy spectrum generated in SOBP beam moderator

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1. Introduction

Recently, heavy ion therapy shows good result on the cancer treatment. Information is lacking on the measurements of secondary neutron doses. Therefore, the secondary neutron dose from carbon ion beam is investigated in recent year. In this research, measurement of the secondary neutron energy spectrum generated in SOBP moderator.

2. Methods

The experiment has been performed at the biological beam line of HIMAC, National Institute of Radiological Science, Chiba. A 290 MeV/nucleon carbon SOBP beam (6cm, 10cmf) was used for this experiment. The secondary neutrons were measured by a liquid scintillation counter with the TO-F technique. Furthermore, Monte Carlo calculation with PHITS code was carried out to simulate the secondary neutron energy spectrum.

3. Results

Neutron event rates of the SOBP moderator ON/OFF shows 2.5:1. This shows that neutrons were generated in the SOBP moderator. The neutron spectra both of measurements and PHITS simulation were obtain.

4. Conclusion

In this research, it is clarified that secondary neutrons produced in SOBP moderator are contributed to therapeutic irradiation. The secondary neutron spectrum can be simulated by PHITS.

In future microdosimetric studies for measurements and simulation will be carried out and neutron dose will be discussed.

Development of Handy Gamma-ray Spectrometer

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Conventional Gamma-ray Spectrometers often combine a scintillator with a photo-multiplier tube (PMT) or a photo diode (PD). However, PMT is large and needs a high operating voltage about 1000 V. PD or APD(Avalanche photo-diode) is sensitive to external electrical noise and its energy resolution is bad at room temperature.

Then, we use MPPC (multi-pixel photon counter) instead of PMT or PD/APD. MPPC is being developed recently, it is small, is less sensitive to electrical noise, and can operate at low voltage of about 70 V. This enables us to develop a Handy Gamma-ray Spectrometer combined with scintillators. If this is achieved, it will be used at households and schools to measure and study gamma-ray radiations.

Currently, we achieve an energy resolution of 9.8 % (@662 keV) at room temperature, by using MPPC with CsI(Tl) scintillator. We develop a compact electric circuit system to supply high voltage to MPPC and read out MPPC signals to make a energy spectrum and to display it.

In this presentation, we present an introduction and experimental results.

Study on the Damage Detection System by Image Analysis

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The efficient method to detect the damage to the structure is important to minimize the disaster related to the radioactive material. Visual inspection is the key process in damage detection, however the result is dependent on the individual skill of engineers.

In this paper, I would like to introduce our system of the damage detection for the road pavement by image analysis. Figure 1 shows an overview of the damage detection system. From snapshot images by a vehicle camera, this system finds the damaged sites and identifies the type of damage in real time.

Figure 2 shows the outline of the image analysis. First, the system classifies the features in each key point of the learning image. The frequencies of key points in each category (features) are summarized as the histograms. Then, in practice, for the new input image, the system compares the histogram for the new input images and that for the learning image. Thus, the system can identifies existence of damage and the type of damage without depending on engineer’s personal skill.

The system is now under the feasibility study. This method can be applied not only for the road maintenance but also for the maintenance of nuclear power plant and the structures to keep the radioactive material in future.

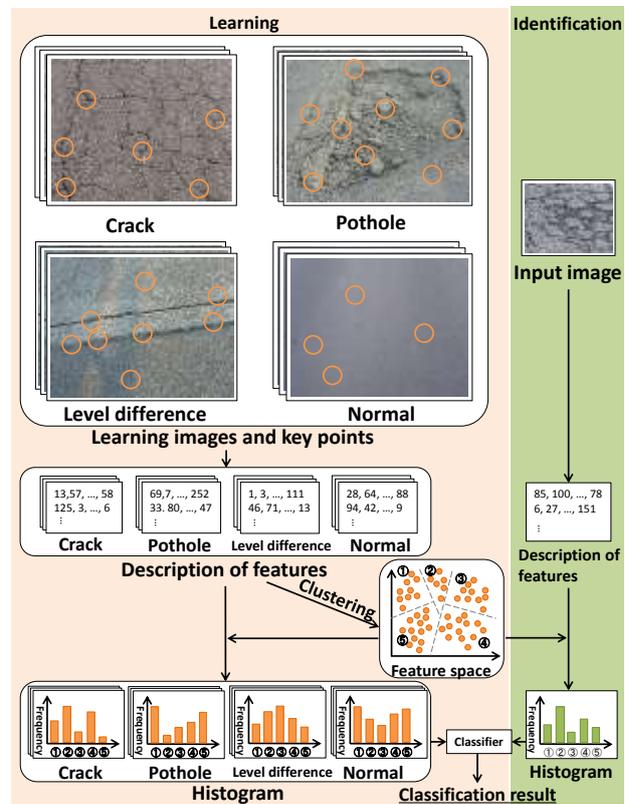


Figure 2 Outline of the image analysis

Development of Cutoff Layer Used for Coastal Disposal Facility of Wastes Contaminated by Radioactive Cesium

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A large amount of wastes contaminated by radioactive cesium generated due to the Great East Japan Earthquake. Because radioactive cesium in wastes must not be flowed out before they become the safe radiation level, the clay layer that have low hydraulic conductivity and adsorption capacity is developed. The purpose of this study is investigating hydraulic conductivity and adsorption capacity of marine clay mixed with bentonite in various mixing proportion. Fig.1 is shown approach of development for cutoff layer.

The laboratory test is carried out with the consolidation and permeability testing apparatus(Fig.2). The consolidation test is carried out to the point of 20kPa and hydraulic conductivity is valued from test result. After the consolidation test is completed, the permeability test is carried out by measuring the flow of cesium solution. The concentration of cesium before and after the flow through clay layer is measured and the adsorption capacity of clay is measured.

In addition, the shaking test is carried out to measure maximum adsorption. The sample is shaken with cesium solution for an hour. After shaking, the sample is centrifugalize for and the supernatant fluid is picked. By measuring the concentration of the liquid, the maximum adsorption of the clay mixed with bentonite is known.

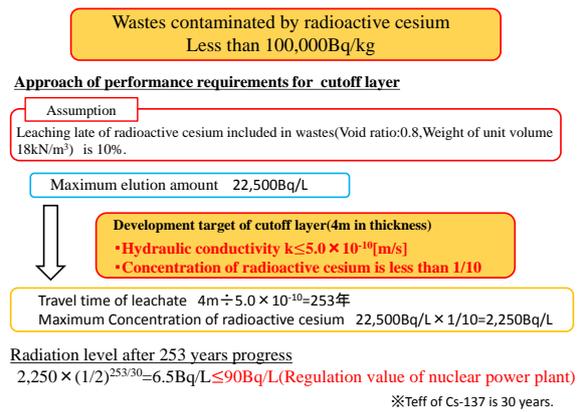


Fig.1 Approach of development for cutoff layer

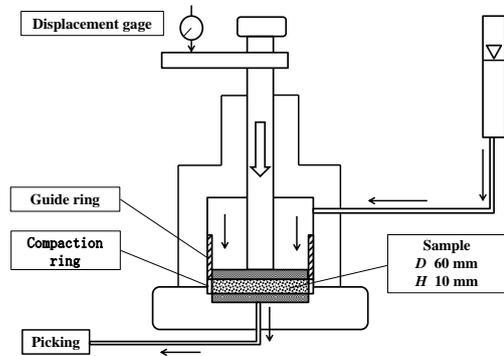


Fig.2 Consolidation and permeability testing apparatus

Research Proposal: Transfer of radionuclides from plants to insects in galls

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INTRODUCTION

In this work the transfer behavior of the radionuclides from the Fukushima Dai-ichi Nuclear Power Plant accident in March 2011 is investigated with galls. Part of the radionuclides in forests, especially in soil, might transfer from soil to plants and then circulate in ecosystem. To estimate the contamination of radionuclides in forests, the purpose of establishing the model of radionuclide transfer is necessity.

AIM

The aim of this study is to investigate the transfer behavior of radionuclides from plants to insects in galls.

MATERIALS AND METHODS

Sampling area

The study area is in Soma City and Minami-Soma City.

Radiometry

Gamma-rays from samples are measured with a low background Ge-detector.

To obtain autoradiographs, use an imaging analyzer.

Statistical analysis

To determine concentration differences between the various factors, statistical analyses are carried out.

EXPECTED OUTCOMES

It is possible that this study would shed further light on the mechanism of radionuclide transfer from plants to insects.

The outcome of these investigations will be helpful to develop the radionuclide transfer model in forests.

Activity as a physical therapist for prevention of disuse syndrome in the General Hospital in radiation disaster suffering of Minami Soma City

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Background

Minami Soma City was strongly affected by the radiation disaster after the Great East Japan Earthquake on March 11, 2011. Many of the medical staff had evacuated from the area, and as a result bringing in supply and medical treatment was difficult.

Purpose

We had worked as a member of the volunteer team at the General hospital in Minami Soma City. The main purpose of our activity was to give patients who need medical treatment and prevent their disuse syndrome such as cardiovascular vulnerability, obesity, musculoskeletal fragility, depression.

Results/Activity

There were more than 80 inpatients there with a capacity of 230. A number of Full-time physical therapists decreased from 13 to 3 because of evacuation. We had given physical therapy including exercises for improving muscle strength and joint range of motion and practices for activities of daily living. It had contributed to prevention of disuse syndrome.

Conclusion

Many inpatients had no choice but to discharge to temporary housing. There are more than 5,000 evacuees there now, and they may cause disuse syndrome due to inconvenient and inexperienced circumstance.

Therefore it is important for patients in disaster areas to continue to take medical treatment through before and after discharge.



Association of hepatitis C virus infection with mortality
in patients on chronic hemodialysis

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【Aim】 The prevalence of hepatitis C virus (HCV) infection is high in patients who are on chronic hemodialysis. We conducted a prospective cohort study of 3,087 patients who were on chronic hemodialysis from 9 dialysis facilities in Hiroshima, Japan to investigate the role of HCV infection in the mortality of these patients.

【Method】 Patients were recruited from 1999 to 2004. We investigated when they instituted dialysis, and the date and cause of death by using questionnaire in 2010. HCV infection was screened by real-time polymerase chain reaction. The Cox proportional hazards model was used to estimate the odds of death.

【Results】 433 patients (14.0%) were positive for HCV RNA. The mortality of patients were positive for HCV RNA was significantly higher than HCV RNA-negative-patients ($P < 0.001$). However, infection of HCV was not risk for death (adjusted relative risk (aRR)=1.08; 95% confidence interval [CI], 0.92 to 1.27; $P = 0.335$) after adjusting for confounding variable. Patients who had diabetes were at increased risk for death compared with non-diabetic patients (RR=1.74; 95% CI, 1.14 to 2.58; $P = 0.012$).

【Conclusion】 We conclude that HCV infection didn't increase the risk for death during the study period compared with those not infected.

Injuries related to restoration activities at the Fukushima Daiichi Nuclear power Station.

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Background: Following the Fukushima Daiichi Nuclear power station (1F) accident, the re-establishment of temporary cooling facilities for the damaged 3 reactors and the spent fuel pool of the Unit 4 reactor building was put in the first place. We reported here injuries related to the restoration activities at 1F.

Methods: We analyzed data of the published report from Tokyo Electric Power Company (TEPCO) from March 11th 2011 through June 30th 2012.

Results: During the operations, a total of 67 workers sought emergency medical care in March 2011. Among these, 44 workers complained of medical problems such as general fatigue and sickness which were irrespective of levels of irradiation dose. A total of 261 workers had been treated at the 1F until June 30st 2012. Among these, trauma accounted for 131 cases, most of them were observed in the first 5 months after the accident occurred (from March 12 through July 2011). Regarding severity of trauma, only one patient exceeded Injury Severity Score of 15. Fortunately, no trauma death was reported.

As for radiation exposure, only 6 cases were complicated with radiological contamination, all of which occurred in March 2011. From March 11th 2011 through March 31st 2012, a total of 19,594 workers were involved in the restoration operations at the 1F. Ninety six percent of these workers were exposed to less than 50 mSv. Total irradiation dose greater than 200 mSv were observed in 9 workers. Of these, 2 workers were exposed to greater than 600 mSv with 678 mSv the highest of all. All of those whose irradiation doses were greater than 100 mSv were exposed soon after the accident occurred.

Conclusion: Most of the injuries related to the restoration activities at 1F were classified as minor, and radiation exposure was limited less than the levels which associate with acute radiation syndrome.

Roles of Hiroshima University in the early phase of radiation emergency medical managements in the Fukushima Daiichi Nuclear Power Station accident

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Hiroshima University, which has been designated as a tertiary radiation emergency medical care facility, is assigned the task of dispatching a radiation emergency medical team in the event of nuclear accidents. On March 12th, our team was dispatched to Fukushima by the Self-Defense Force helicopter with a team from the National Institute of Radiological Sciences. Soon after the accident, all radiation emergency medical facilities inside the 20 km radius from the Fukushima Daiichi Nuclear power station (1F) were completely closed. The first mission in Fukushima was to set up a medical response HQ just as quickly as possible so as to deal with the emergency radiation exposures and related injuries. The issues discussed included decontamination criteria for evacuees, evacuation of patients left inside the 20 km radius from the 1F, and re-establishment of the radiation emergency medical system for workers who were involved with restoration activities at the 1F.

Although most of the residents had left by March 13th, more than 840 patients remained left inside the 20 km radius from the 1F. As the situation of the damaged nuclear power station became more unstable, the government ordered an immediate evacuation of all patients on March 14th. Unfortunately, 50 patients were killed during this evacuation. The causes of death were presumably hypothermia, deteriorating underlying medical problems and dehydration.

Two hydrogen explosions took place on March 12th and 14th. A total of 15 workers sustained injuries. Marked difficulties were encountered to allocate these patients to hospitals because strong concerns over radiological contamination existed among health care workers in Fukushima. Fortunately, no serious injuries or acute radiation syndrome were reported in these explosions.

Efforts for re-establishing the radiation emergency medical system had been made by cooperation of governments and various organizations, and Hiroshima University played the central roles in coordinating these activities.

How can we educate school children to participate in the activities to solve environmental problems ?

Mieko DOI

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Background

After the nuclear accident, a new environmental education initiative such as the creation of "instructional materials for radiation" started. The goal of environmental education is tied to the behavior to solve environmental problems. Children learned through environmental education of "knowledge" does not necessarily lead to the "behavior" to solve environmental problems.

Study purpose

The purpose of this study is to examine how to build an educational process to reach to the behavior to solve environmental problems.

Method

- (1) Questionnaire survey(QS) for university students on environmental issues,
- (2) Investigation of Educational Materials used in the school

Results

- (1) QS were carried out for university students in China, Malaysia and Japan, which clarified that the gap among "behavior" and "knowledge" of environmental problems is distinguished at students of Hiroshima University, Japan.
- (2) Educational Materials collected have shifted from learning with a focus on knowledge to the description to support active learning and behavior.

Conclusions

The subjects in environmental education are diverse, including recycling, resource and energy conservation. The "nature and utilization of radiation" and "effective use of energy resources" evolved is an important school education. The results above show the direction of expected children's activities and support required for behavior.

Function of RAD18 on radioresponse

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DNA damage can be induced by environmental insult as well as endogenous metabolism. To maintain genome integrity, the cells have evolved various DNA repair systems. Post-replication repair is one of the repair systems and referred to as DNA damage tolerance. Post-replication repair pathway can bypass DNA lesions to restart DNA replication without removing the DNA damage. This process involves template switching and translesion DNA synthesis. RAD6-RAD18 complex plays the important role to regulate its pathway. It has been reported that absence of RAD18 sensitizes to a variety of DNA damaging agents such as ionizing radiation and display enhanced genomic instability.

In this study, in order to better understand the role of post-replication repair on radioresponse and its molecular mechanisms, the cellular responses to ionizing radiation were investigated using RAD18 knockdown human cell line.

Our results demonstrated that RAD18 contributes to signal transduction pathway after radiation exposure. It is assumed that post-replication repair plays a critical role to maintain genomic stability after radiation exposure.

The effect of intragroup and intergroup status on evaluation of ingroup and outgroup.

— Focused on the moderating effect of intergroup relation. —

Hitomi Sugiura^{1,2} and Kiriko Sakata².

1. JPSP Reseach fellow. 2. Hiroshima University



We investigated whether intergroup relations moderated the interaction between intergroup and intragroup status on outgroup derogation. A previous study by Sugiura and Sakata (2009) showed that low intragroup status members in high status groups (L-H member) and high intragroup status member in low status groups (H-L member) were inclined to show outgroup derogation. We presumed that intergroup comparisons underlie this effect. We predicted that intergroup relationships would moderate this interaction effect, because people have a tendency to engage in intergroup comparison in competitive situations. Participants (N=120) were classified based on their course. Two factors related to their status were manipulated by false feedback of task1. They were then asked to evaluate impressions of ingroup and outgroup members as task2. As predicted, results indicated L-H and H-L members that perceived intergroup relationships as being competitive, evaluated the competence of outgroup members as being significantly low. This finding suggests the importance of the comparison targets in outgroup derogation.

Acquired expression of c-Cbl Q367P mutation induces myeloid cell proliferation

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c-CBL functions as an E3 ubiquitin ligase and negatively regulates tyrosine kinase-induced intracellular signaling. Recently, mutations of the *c-Cbl* gene were identified in a substantial portion of hematopoietic malignancy mainly of myeloid lineage. This suggests that dysfunction of c-CBL is implicated in the pathogenesis of the disease, but the precise leukemogenic mechanism(s) remains elusive. To gain insights into this issue and to create a novel animal model for mutated c-CBL-harboring leukemia, we generated conditional knock-in (cKI) mice that express wild-type c-CBL at steady state and in turn express c-CBL with Q367P mutation (c-CBL^{Q367P}) upon Cre activation. After induced expression of c-CBL^{Q367P}, the cKI mice rapidly exhibited leukocytosis with expansion of myeloid cells. The spleen was massively enlarged with proliferation of immature and mature myeloid cells, and the bone marrow was hypercellular with predominance of myeloid cells. These results provided *in vivo* evidence that acquired expression of c-CBL^{Q367P} conferred a proliferative advantage to myeloid lineage and resulted in uncontrolled proliferation of myeloid cells. Our cKI mice represent a novel and useful animal model for investigating the leukemogenic mechanisms mediated by mutated c-CBL.

KIF2A phosphorylation by PLK1 regulates primary cilia disassembly

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[Background]

A primary cilium is an antenna-like microtubule-based organelle on cell surface, and functions as a sensor for extracellular signaling. While primary cilia formation occurs in G0 phase, cilia disassembly begins when G0 quiescent cells re-enter a proliferative phase. It was recently shown that mitotic kinase PLK1 suppresses cilia formation. However, little is known about the molecular mechanism of PLK1-mediated ciliogenesis.

[Purpose of research]

We focused on kinesin protein KIF2A, which has an activity of microtubule depolymerization, and studied its functional role in the PLK1-mediated ciliogenesis.

[Material and method]

To determine a phosphorylation site on KIF2A by PLK1, *in vitro* kinase assay was performed. PLK1-specific phosphorylation of KIF2A during ciliogenesis was studied by immunostaining of hTERT-RPE1 cells using anti-phospho-KIF2A antibody. Ciliogenesis was analyzed in the cells after transfection of KIF2A mutants or KIF2A siRNA.

[Result]

Threonine 554 on KIF2A was identified as a phosphorylation site by PLK1. Then, we raised anti-phospho-KIF2A antibody against phosphorylated T554. Immunostaining analysis revealed that KIF2A was localized to the centrioles during ciliogenesis while PLK1-specific phosphorylation on KIF2A was increased at the mother centriole when the cells enter the proliferative phase. siRNA-mediated KIF2A knockdown increased the primary cilia length.

[Conclusion]

PLK1 phosphorylates threonine 554 on KIF2A and promotes primary cilia disassembly possibly through an increased microtubule depolymerase activity of KIF2A.

HBp17/FGFBP-1 Expression is Down-regulated by $1\alpha, 25(\text{OH})_2\text{D}_3$ in Oral Squamous Cell Carcinoma Cell Line: Implication on its Biological Role towards Growth Regulation

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[Background] FGF-2 is the prototypic member of a family containing at least 23 structurally-related polypeptide growth factors. It is expressed ubiquitously in a variety of tumor cells including oral squamous cell carcinomas. *In vitro*, FGF-2 is a potent mitogen for different cell types, including vascular endothelial cells, fibroblasts and cancer cells such as squamous cell carcinomas. *In vivo*, FGF-2 is a potent inducer of angiogenesis and has pleiotropic effects both on development, differentiation in various organs, and tumorigenesis. FGF-2 is secreted despite lacking a leader sequence, which targets intracellular proteins for secretion to the extracellular environment, and externalized FGF-2 needs to be released and solubilized from the extracellular matrix. We initially isolated heparin-binding protein of 17 kDa which was found to bind FGF-1 and FGF-2 in a non-covalent and reversible manner in 1991 from the medium conditioned by human epidermoid carcinoma A431 cells and designated the protein as heparin-binding protein 17 (HBp17). Owing to its capacity to bind FGFs, HBp17 was renamed fibroblast growth factor-binding protein-1 (FGFBP-1). Binding of HBp17/FGFBP-1 to FGF-2 mediates the release of immobilized FGF-2 from the extracellular matrix allowing it to reach its receptor, suggesting that HBp17/FGFBP-1 serves as an extracellular switch molecule for FGF-2. Recently, it was reported that up-regulation of HBp17/FGFBP-1 was found in various tumors, including head and neck, skin and colon cancers. In this paper, we proposed the possibility to restrain the expression of activated FGF-2 in cancer cells, by manipulating expression of its chaperone, HBp17/FGFBP-1 by $1\alpha, 25(\text{OH})_2\text{D}_3$ (VD).

[Purpose] To investigate the effect of VD on HBp17/FGFBP-1 and FGF-2 expression in OSCC cells.

[Methods] OSCC cell line (UE: HO-1-u-1), established in our laboratory has been used in this study. The cells were treated periodically with VD (40nM) in serum-free culture. Both mRNA and protein expression for HBp17/FGFBP-1 and FGF-2 were quantified using qRT-PCR and Western blotting (WB). VDR RNAi-transfected UE cells (siVDR) were used to determine the role of VDR upon the VD treatment on HBp17/FGFBP-1 expression. ELISA was performed to determine soluble HBp17/FGFBP-1 and FGF-2 protein released into the conditioned media.

[Result] Treatment of OSCC cells with VD (40nM) suppressed the release of HBp17/FGFBP-1 and FGF-2 in the conditioned media. Inhibition of HBp17/FGFBP-1 expression was also demonstrated by qRT-PCR, WB and immunofluorescence analysis upon VD treatment. Besides these, VD does not have direct effect on the synthesis of FGF-2 protein. Thus, it was speculated that down-regulation of HBp17 expression resulted in the change on the level of soluble FGF-2. In addition, the data using siVDR implied that HBp17/FGFBP-1 inhibition by VD was mediated by VDR.

[Conclusion] The ability of VD to suppress HBp17/FGFBP-1 and FGF-2 expression in OSCC depicts another anti-cancer mechanism by VD and as well showing these molecules could be the target molecule in cancer therapy by VD.

Chromosome abnormalities in human peripheral blood after low-dose ionizing radiation

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The analysis of dicentric chromosomes in human peripheral blood lymphocytes (PBLs) by Giemsa staining is the most established method for biological dosimetry. However, this method requires a well-trained person because of the difficulty in detecting aberrations rapidly and accurately. We applied a fluorescence in situ hybridization (FISH) technique, using telomere and centromere peptide nucleic acid (PNA) probes, to solve this problem in biological dosimetry. A comparison by a well-trained observer found that FISH analysis of PBLs for the dose estimation was more accurate than the conventional Giemsa analysis in samples irradiated at high doses. We could also apply the PNA-FISH analysis for the detection of the chromosome abnormalities in PBLs induced by low dose ionizing irradiation ($\leq 100\text{mGy}$). These results show that FISH analysis with centromeric/telomeric PNA probes could become one of the standard methods for biological dosimetry in radiation emergency medicine.

An improved method for analyzing ionizing radiation-induced chromosome aberrations

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Radiation induces DNA damage sometimes fail to be repaired appropriately leading to the rejoining of broken DNA ends incorrectly. The mis-repaired DNA produce chromosome aberrations, which becomes critical when such chromosome aberrations activate oncogenes. Thus, a quickly and accurately evaluation method for radiation induced chromosome aberrations is very important for both clinical radiation dosimetry and the basal molecular mechanisms of aberrations study.

Giemsa staining is the most established method especially to evaluate the chromosome aberrations in human blood lymphocytes. However, this method is inefficient and error-prone as it simply marks the chromosome body and difficult to detect aberrations accurately and rapidly.

Here, we applied a fluorescence in situ hybridization (FISH) technique, using telomere and centromere peptide nucleic acid (PNA) probes to solve the most defects of Giemsa staining and get more accurate and highly reliable result. To overcome the most time consuming step and save more time in this method, we used an automatic metaphases search and images taking system-Metasytem. In this way, we established an accurate and high performance evaluation method for radiation induced chromosome aberrations by PNA-FISH combine with Metasytem. Moreover, we applied this newly established method to examine the chromosome abnormalities in human cell lines after ionizing irradiation. Involvement of repair factors in the induction of chromosome abnormalities after ionizing irradiation will be discussed.

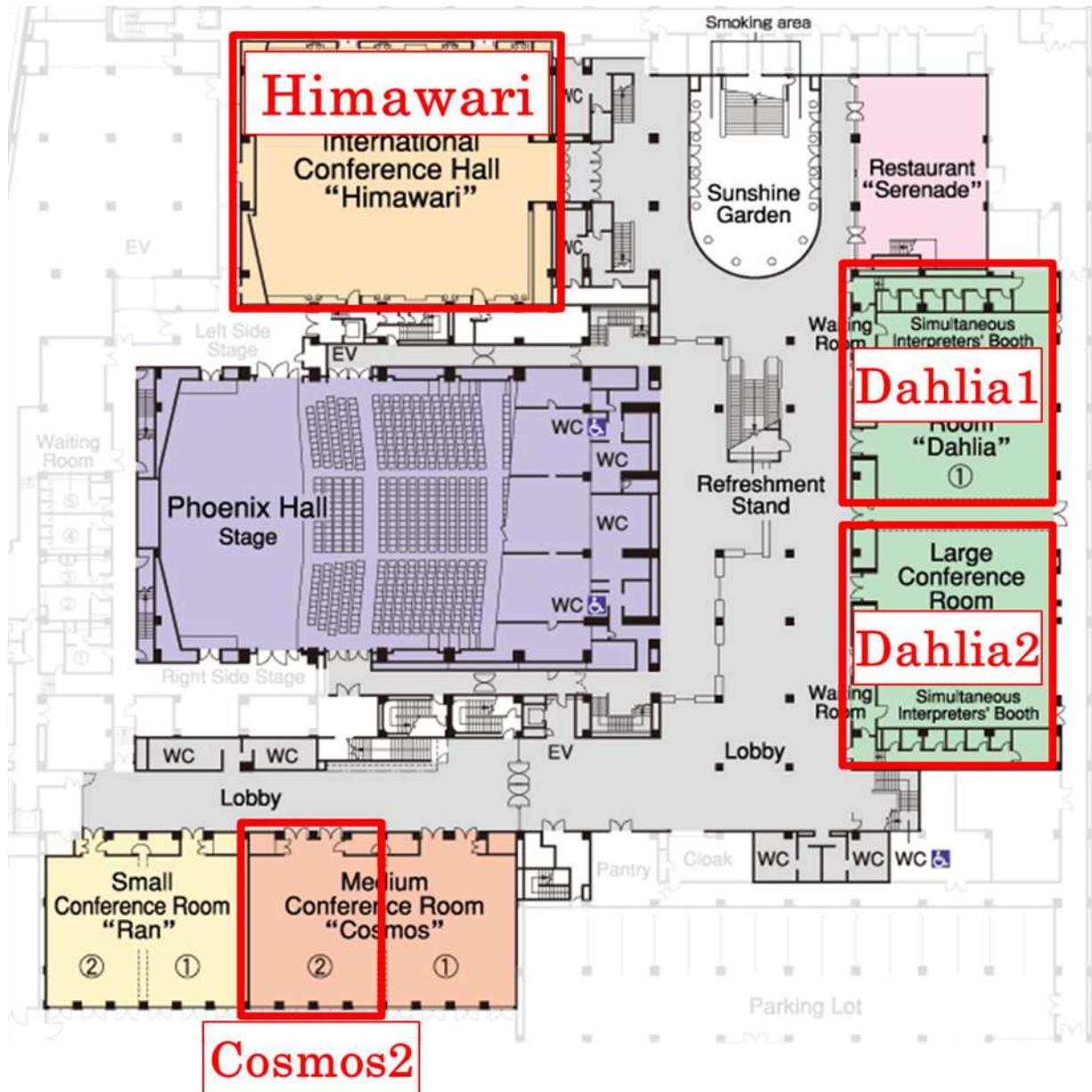
Map
of
Hiroshima City
and
Symposium Floor

Map of Hiroshima central part



- ① Hiroshima Station
- ② International Conference Center Hiroshima (This symposium venue)
- ③ Hiroshima Peace Memorial Museum
- ④ Peace Memorial Park

**International Conference Center Hiroshima
Floor map of second basement**



Himawari

- Opening Ceremony
- Keynote Address
- Lectures

Cosmos 2

- Reception

Dahlia 1

- Panel Discussion
- Closing Ceremony

Dahlia 2

- Poster Session

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