Masashi Kusakabe, Ph.D.
Director, Fundamental Technology Center

[Outline of Research Career]

In 1980 upon completion of his Ph.D. research in Hokkaido University, Dr. Kusakabe moved to University of Southern California, Los Angeles, to study the behavior of radionuclides in the ocean. In particular, his research focused on cosmogenic nuclides such as $^{10}$Be and U-Th series radionuclides. In 1997, he joined the Japan Agency for Marine-Earth Science and Technology (then called Japan Marine Science and Technology Center), where he studied the carbon cycle in the ocean by using radionuclides. Since 2002, he has been a director of the NIRS Nakaminato Laboratory for Marine Radioecology in Ibaraki Prefecture. Since 2008, he has been concurrently Director of the Fundamental Technology Center which now occupies a considerable amount of his workload.
Contact point: masashi@nirs.go.jp
Objectives
The Fundamental Technology Center was newly established in 2006 to support and promote the wide variety of research activities done at NIRS. It consists of two departments with seemingly different natures, the Department of Safety and Facility Management and the Department of Technical Support and Development. They work sometimes in complementary manner to each other. While the Center provides state-of-art technology to and helps NIRS scientists, it also ensures the safety of the working environment. An outline of the Center activities and structure follows in the next section.

Overview
The Center consists of one office, two departments and seven sections. Figure 7-1 shows the organizational structure of the Center. The Planning and Promotion Office is responsible for planning and management of work in the Center. It also manages common use facilities. In addition, the Office sponsors meetings to facilitate the technical development of NIRS and to provide a bridge between scientists and technologists.

The Department of Technical Support and Development consists of three sections: (1) Technical Advancement of the Radiation System Section; (2) Radiation Measurement Research Section; and (3) Laboratory Animal Science Section.

The Department of Safety and Facility Management consists of four sections; they are shown below with their operations.

(1) Safety and Risk Management Section
- Planning and promotion of safety assurance
- Training of employees on safety issues
- Assurance of safety on campus
- Protection of the public from nuclear power accidents

(2) Radiation Safety Section
- Legal management of radiation and radioactive materials
- Radiation exposure management
- Training of employees who deal with radioactive materials and radiation
- Assurance of safety with respect to radiation
- Management of radiation related facilities and radioactive waste

This Section includes the subdivision, Nuclear Fuel Control Office, which is concerned with the management of radionuclides used in nuclear fuel.

(3) Safety Control Section
- Planning of fire control measures
- Establishing safety controls of gene recombination experiments and hazardous chemicals
- Safety assurance in working environments

(4) Facility Management Section
- Management of energy consumption, working environments, and general wastes
- Construction and maintenance of buildings

Fig. 7-1 Organization of Fundamental Technology Center.
Hitoshi Imazeki, Ph.D.
Director, Department of Technical Support and Development

(Outline of Research Career)

Our department staff consists mainly of technologists who support researchers in the other research centers in NIRS and domestic and international institutions with knowledge, experiences and technologies. Inherited or newly developed technologies have been enhanced in order to provide better facilities, devices and animals for various research projects in biology, medical and physics. Our department is composed of three sections, Technical Advancement of Radiation Systems Section, Radiation Measurement Research Section and Laboratory Animal Sciences Section.

Contact point: b_imazeki@nirs.go.jp
Technical Advancement of Radiation Systems Section

This section provides technical supports for radiobiological researchers along with advancing developments of radiation systems. This section provides a variety of radiation sources, such as X-ray, gamma-ray, and neutron sources, and our mission is to ensure the quality of those radiation fields, such as dose, dose rate, and field uniformity. We also have two electrostatic accelerators. The original one is called PASTA (PIXE Analysis System and Tandem Accelerator), which accelerates protons and helium ions for multi-elemental analysis in biological and other environmental materials. There is a beam line is installed in PASTA, which is called SPICE (Single Particle Irradiation system to Cell) and this is a microbeam irradiation system exclusively designed for radiobiological studies such as research concerning radiation risk assessments. The second electrostatic accelerator facility is called NASBEE (Neutron exposure Accelerator System for Biological Effect Experiments), and it generates a neutron beam at an average energy of 2.0 MeV at high dose rate. Neutron beams are introduced into the SPF-conditioned room, which enables researchers to work with radiation-induced carcinogenesis using mice. These accelerator facilities are available for collaborative research projects. We also provide technical assistance for the single cell analysis sorter (flow cytometer), the XRF (X-ray fluorescence) analysis system and other analysis systems that are highly technical and require experience for their successful operation.

Radiation Measurement Research Section

Dosimetry and radiation measurements are required for radiation biology and physics research projects. In order to respond to this need, we characterize the radiation fields and provide data of radiation parameters using radiation dosimeters and detectors. Also, brand-new detectors and dosimeters are developed utilizing new technologies.

Our section is composed of 3 permanent staff members, 2 full time technical and scientific staff members, 1 post-doctoral fellow and 3 support staff members. And, many national and international collaborators support our work as well.

Laboratory Animal Science Section

It is absolutely necessary to use experimental animals in animal experiments to advance biomedical and radiological research and education. There are 11 institutes using experimental animals in Japan and our section has various animal species, for example mice, rats, Mongolian gerbils, rabbits, and monkeys. Those animals are humanely taken good care of by our staff. Our staff is composed of nine permanent members, five animal technicians (including two veterinarians), four clerical workers and 50 non-permanent staff members.

In April 1999, the guidelines concerning the care and control of experimental animals were revised. All animal researchers at NIRS must adhere to these new guidelines. The Laboratory Animal Care and Use Committee (LACU) acts as the cornerstone of our system of self-regulation. LACU has to examine animal research protocols in order to ensure that all animal research projects are in compliance with the guidelines. No animal research projects can be carried out without approval by the LACU.
7.2. Current status of the microbeam irradiation system for mammalian cells, SPICE

INTRODUCTION

Single-cell microbeam irradiation systems have become significant tools in the field of radiation biology. Recently, many microbeam facilities have been developed, and are available for biological research worldwide. Also in Japan, there are many microbeam facilities with different types of radiation sources that are now available for biological studies, such as low-dose effects, hyper radio-sensitivity, bystander effects and so on. The single particle irradiation system (SPICE) of NIRS generates 3.4 MeV protons with an approximately 2 μm diameter beam, and is the only microbeam irradiation system in Japan with low-LET parti-cles irradiation. SPICE is currently operative for biological studies.

This year, the “8th International Workshop on Microbeam Probes of Cellular Radiation Response” was organized and held at NIRS and the Extended Abstracts were published (8th International Workshop on Microbeam Probes of Cellular Radiation Response, Extended Abstracts. J. Radiat. Res., 50: Suppl., A81-A12, 2009).

There were a total of 113 participants, including researchers from overseas. Recent developments and biological research in microbeam facilities in Europe, U.S. and Asia were also reviewed in the workshop. This workshop series has been highly successful in bringing together groups interested in developing and applying micro-irradiation techniques to the study of cell and tissue damage by ionizing radiations and provided a forum to assess the current state of microbeam technology and current biological applications, and to discuss future directions for development, for both technological and biological aspects. (See poster, Fig. 7-2)

Fig. 7-2. Poster of the 8th International Workshop on Microbeam Probes of Cellular Radiation Response.

OUTLINE OF SPICE

The electrostatic accelerator facility of NIRS supplies protons and helium ion beam by a Tandetron accelerator. In this facility, there are four beam lines, and three horizontal beam lines are available for PIGE analysis PASTA. The fourth beam line, SPICE is a vertical beam line, the beam of which is transported upward after passing by a 90-degree bending magnet installed in the middle of the microbeam scanning PIGE beam line. The main characteristic of SPICE is that a beam is focused by a Q-magnet lens (Oxford Microbeam Ltd.). The number of protons traveling through the cells is counted using a scintillation detector equipped on the microscope system which is set above the cell dish. The computer that controls the voice coil motor stages gives a high-speed trigger pulse to the beam deflector to turn the beam on and off. It is possible to irradiate from a single to an arbitrary number of protons per position or cell. Cells are dyed with Hoechst 33258, and their fluorescent image is captured with a CCD camera. This system computes the X-Y coordinates of the cell position according to their fluorescence. All of the irradiation procedures can be performed automatically after setting some parameters, such as a preset number of protons.

BEAM-SIZE MEASUREMENT USING CR-39

Beam size has been measured by the plastic track detector, CR-39 (HARTZLAS TD-1). A thin CR-39 film was adhered to a cell dish, and then the dish was set on the stage. The image of Fugaku 36t drawn by Katsushika Hokusa was reprinted as a microbeam drawing as shown in the Workshop poster (see Fig. 7-1). This microbeam drawing was performed automatically according to the text file of a preset number of protons and the X-Y coordinates of the sample stage position, which consisted of 14,000 irradiation positions. This system allows from 6 to 8 positions to be irradiated per second, therefore the irradiation of CR-39 shown in figure was accomplished within approximately 30 min.

FUTURE AIM AND DEVELOPMENT

We have developed the microbeam irradiation system, SPICE. An approximately 2 μm diameter beam was real-ized and the 5 μm diameter beam is now available for daily irradiation. Irradiation with a single proton can also be per-formed and the maximum speed for cell irradiation is over 400 cells per minute. Most of the irradiation procedures can be performed
automatically by setting some parameters. Further improvements are underway, such as an off-line microscopic system for post-irradiation biological analysis, improvements of targeting accuracy and reduction of the beam size below 2 μm in diameter.

SPICE and PASTA are now available as an open facility for collaborative research projects. Contact infopixe@nirs.go.jp for beam time schedules and other detailed information.

**Major publications**

4) T. Konishi et al., *Nucl. Inst. and Meth. B*, in press
5) H. Imaseki et al., *Int. J. PIXE*, 10: 77-90, 2001
6) T. Ishikawa et al., *Nucl. Inst. and Meth. B*, in press
7.3. Research Work in the Radiation Measurements Research Section

Yukio Uchihori, Ph.D.
Heard, Radiation Measurements Research Section

(Outline of Research Career)

Dr. Uchihori received a Ph.D. from Osaka City University in 1995 for his study on cosmic-ray physics at high mountain and deep underground. He joined extremely high energy cosmic-ray experiments as a fellow in Institute for Cosmic Ray Research, Tokyo University. In 1996 he moved to NIRS and worked on space radiation protection and measurement. He worked in the MEXT (Ministry of Education, Culture, Sports, Science and Technology) in FY 2006 and in the planning section in NIRS.

Contact point: uchihori@nirs.go.jp
Objectives

Research work done in Radiation Biology and Physics needs reliable dosimetry or measurement data in the radiation field. Our members support the activities of NIRS researchers using conventional and/or the latest radiation detectors. And, we also propose new research topics in various new radiation fields like micro-beam and low dose neutron facilities to biologists and physicists in order to open new areas of the sciences.

Several detectors have been developed by leading-edge techniques and calibrated in various radiation fields like that of HIMAC, cyclotrons, neutron fields, precise radiation sources, and so on. Not only detectors themselves but also analysis methods including hardware and software, simulation code and electronics have been developed.

Dosimetry of space radiation is another object of interest and several detectors for space radiation measurements were developed. Under a collaboration with the Institute of Bio-Medical Problems (IBMP), Russian Academy of Science, there were several opportunities to measure space radiation in the International Space Station (ISS). Also, the international intercomparison program of space radiation detectors, the ICCHIBAN (InterComparison for Cosmic-rays with Heavy Ion Beams At NIRS) Project, is ongoing to understand and standardize detectors for space radiation dosimetry.

Progress of Research

Passive detectors (Nakahiro Yasuda, Satoshi Kodaira, Shuya Ota, Iva Jadmickova, Mieko Kurano, Hajime Kawashima, Hisashi Kitamura, Yukio Uchihori)

Development of a fluorescent nuclear track detector technique

A novel fluorescent nuclear track detector (FNTD) was verified as a possible spectroscopic technology for heavy charged particles with wide range linear energy transfer (LET). The technique uses a luminescent aluminum oxide single crystal having aggregate oxygen vacancy defects and doped with Mg (Al₂O₃:Mg) as the detector in combination with a laser scanning confocal fluorescence microscope. We found that the lower detection limit for LET in water was less than 0.5 keV/μm (corresponding to 160 MeV protons). A previous study showed the higher limit would be more than 9,000 keV/μm. This indicates that the method has a very large dynamic range for LET measurements, and has enough capability to be applied as a personal monitor for space use. Based on the result, we designed a compact reader for this application as an on board instrument. For further study, we will verify the detector response to a mixed field radiation field such as heavy ions with X/γ ray or high energy neutrons. [Done in collaboration with: Landauer Inc. (USA) and Nagase Landauer Inc. (Japan)]

Development of the new CR-39 detectors for the precise measurement of high LET particles

Precise LET measurement of higher LET radiation is necessary to estimate dose equivalent for astronauts. Recently, the dose contribution of high LET components (> 50 keV/μm) originated from target fragmentation reactions has been discussed. We have developed the new type copolymer detector of CR-39 and DAP resin detectors and the new chemical etching method using PEW solution for control of the detection threshold of LET. The CR-39/DAP copolymer has the unique characteristic to degrade the sensitivity to the high LET particles. The new etching technique using PEW solution could make it easy to control the detection threshold and to improve the charge resolution of high LET particles.

Development of the particle tracking algorithm in CR-39 detectors

A new method to trace heavy ion trajectories in a stack consisting of interleaved CR-39 detectors and target material layers was developed and verified for the use in the precise measurement of projectile charge changing cross sections of heavy ion fragmentation reactions. A high speed imaging microscope with sophisticated track analysis software was utilized to extract the charge information from multiple ion tracks belonging to a single fragmentation event. The projectile total charge changing cross sections for Fe ions on a carbon target was estimated and compared with previous experiments at initial beam energy of 1 GeV/n, and was results were in good agreement with those obtained by other investigators. This method allows precise and fast measurements of the projectile charge changing cross section with higher statistics, and will be applicable to the precise measurement of LET spectrum in particle therapies and space dosimetry.

Measurements of high LET components in space radiation

We conducted a radiation monitoring experiment for passive radiation dosimeters as a part of the BRADOS experiment on the International Space Station (ISS) for 269 days in 2004. In this study, we employed the CR-39 detector HARZLAS TD-1 and verified the variation of the LET spectra for several bulk etch conditions (multi-step) from 5 - 53 mm at the same position as a TD-1 detector. All etch pits were traced at each step of the etching time as shown in Fig. 7-3. Many high LET particles with short range are observed in the CR-39
detector, which are considered to be produced by target fragmentation reactions with high energy protons. They should make a significant dose effect in inner regions of the human body (e.g. bone consisting of Ca).

Fig. 7-3. The same etch pits were traced on several CR-39 detectors using the multi-etching method.

Neutron detectors (Masashi Takada)

Pocket-size dosimeters with long-life batteries are the preferred device in order to measure cosmic-ray neutrons in aircraft with good accuracy. The possibility to measure the neutron exposure doses in the radiation field produced by cosmic rays in aircraft was investigated with these devices. In long haul flights, the dosimeters were observed to give values 10 times larger neutron ambient dose equivalents than those estimated by the EPCARD code.

In order to investigate dosimeters that can meet this requirement, irradiation experiments were done using 18, 30 and 70 MeV proton and 25 MeV/nucleon alpha-particle beams at the cyclotron facility in NIRS. Measured deposited energies in the silicon detector were about 2 to 5 times larger than calculated deposited energies in the original depletion layer. The large discrepancy in energy deposition in the partially depleted silicon detector used in this study is well explained by considering the funnelling effect for high LET particles.

The charge-collection lengths are found to be independent of particle species, energies and stopping powers but dependent on the original depletion layer thickness. An empirical equation as a function of the depletion layer thickness is introduced to calculate the charge-collection length and the deposited energy in the silicon detectors.

The empirical equation will be used to calculate energy responses of personal neutron dosimeters using silicon detectors for neutrons and charged particles in the design of a dosimeter for aircrews that can be used at cruising altitudes although the detector response to neutrons and charged particles cannot be calculated from the deposited energy in the original depletion layer. The equation will be applied to high-energy and heavier particles and electrons because the charge-collection length is independent of particle species, energies and stopping powers.

Energy deposition of X, γ and electron dosimeters would also be calculated.

Scintillation detector (Hidehito Nakamura)

A new method was developed to obtain reliable calibrations using radioisotope sources. This has proven to be a powerful tool to obtain a detector response with high accuracy. Not only conversion electrons but also α particles, β particles, γ rays and X rays from radioisotope sources can be studied with this method. The method was validated with a plastic scintillation plate in the developed clinical scanner CROSS using a 209Bi source and a 137Cs source (Fig. 7-4). With this method, the energy resolution of the plastic scintillator plate was σ = 3.7/E% with E in units of MeV, which is a good energy resolution compared to other plastic scintillator detectors.

The method will be feasible for use not only for scintillation detectors but also for other detectors. There is a possibility that the method reported here will improve calibration methodology for radiation detectors, because it outperforms other methods used for radiation measurement.

FIG. 7-4. Energy spectrum of 976 K conversion electron line from the 209Bi source. It can be seen that the peak is asymmetrical due to loss of the energy deposited in the 209Bi source.

ICCHIBAN program (Yukio Uchihori, Nakahiro Yasuda, Hisashi Kitamura, Satoshi Kodaira)

The 3rd Space Intercomparison Experiment in the Russian Service Module in the ISS was performed within the ICCHIBAN project. In the last fiscal year, the
2nd Space Intercomparison Experiment was performed and this 3rd experiment was planned to research more details of the responses of passive detectors.

For this 3rd experiment, passive detectors (TLD, OSL, CR-39 and so on) from 13 institutes and universities in 10 countries were sent to NIRS and the package which contained these detectors was launched in the ISS with support by the Institute of BioMedical Problems, Russia. These detectors were recovered and distributed to the participants. These detectors have been analyzed and the participants will report these results in the near future.

From March, 2009, a Japanese astronaut was staying for three months, a rather longer period than past Japanese astronauts. And in the near future, Japanese astronauts may stay for longer periods in the space environment for lunar space bases or Mars explorations. For longer stays, we should research radiation effects for humans; some members have joined the Space Radiation Research Unit in the International Open Laboratory in NIRS.

Fig. 7-4. Photograph of a detector package in the 3rd Space-Intercomparison Experiment.

Major Publications


7.4. Laboratory Animal Science Section

Tetsu Nisikawa, Ph.D.
Heard, Laboratory Animal Science Section

Contact point: tnishika@nirs.go.jp
Now, we are carrying out the following research projects.

- **The cannibalism of mouse-strain differences; examining on foster parents eating foster infants.**

  To research the mouse-cannibalism by mothers which nurse foster infants, we compared the incidences among three ICR sub-strains (Slc:ICR, Jcl:ICR, Crlj:ICR), Slc:ddY, and four inbred strains (BALB/c, C3H/He, C57BL/6, DBA/2). Ten mice from each sub-strain were used as foster mothers. Experimental designs were as follows:

  1. Five mother mice nursed only foster infants.
  2. Five mother mice nursed two of their own infants plus 2 to 8 foster infants.

  Three ICR sub-strains nursed three C3H/He sub-strains and three C57BL/6 sub-strains.

  Slc:ddY nursed C3H/HeSlc and C57BL/6/CrSlc sub-strains. Four inbred strains nursed only Slc:ICR. We found 81.1% of infant mice were cannibalized by foster mothers within 24 hours, regardless of the strains of mothers.

  In the case that when Slc:ICR, Jcl:ICR and Crlj:CD1 mice were used as foster mothers and they nursed C3H/He-sub strains, the cannibalism ratios (number of cannibalized infants / number of fostered infants) were 100%, and 20.0 to 56.0%, respectively. In the case that when the same foster mothers nursed three C57BL/6 sub-strains, the ratios were 82.0 to 100%, and 16.1 to 50.0%, respectively. In the case that when Slc:ddY mice were used as foster mothers and they nursed C3H/HeSlc, the cannibalism ratios were 37.0%, and 27.6%, respectively. In the case that when the same foster mothers nursed C57BL/6/CrSlc, the ratios were 86.6%, and 60.9% respectively. In the case that when C3H/HeSlc and C57BL/6/CrSlc mice were used as foster mothers, both 1 and 2 showed the same ratio: 0 to 7.5%.

  In the case that when BALB/c/CrSlc and DBA/2/CrSlc mice were used as foster mothers, both 1 and 2 showed the same ratio: 3.3 to 22.5%.

  Cannibalism ratios of four inbred strains of mice were lower than those of outbred strains of mice in both 1 and 2. As a result, we concluded that inbred strains are more suitable as foster mothers than outbred strains.

- **Establishment of the genetic monitoring system of the mouse using microsatellite markers**

  We established the genetic monitoring system using microsatellite markers of 15 inbred strains of mice. These markers offered good advantages regarding of time, labor, economy, efficiency, validity, and accuracy, compared with the biochemical and the immunological markers.

  This experiment showed that there are chromosomes which are not inspected, and chromosomes which have only one gene locus in themselves. Next, we will use new microsatellite markers to invent them. And this experiment also showed that in a certain microsatellite marker, it is difficult to make judgments, because the sizes of DNA products are not so different from one another. We will exchange the marker for others ones to establish an easier system.

- **An improvement for shortening the operation time of an isolator**

  - **A trial manufacture of a new metal stopper**

    The rubber stopper is used to adhere the inner cover to the sterile lock in a vinyl isolator (VI). We prototyped a new kind of a metal stopper in order to reduce the working time. Then we measured the average times for installing a rubber stopper and a metal stopper respectively.

      Rubber stopper
      3 workers with 2 to 3 years’ experience in handling VIs-----21.6 seconds.

      5 workers with no experience in handling VIs-----46.4 seconds.

      Experienced workers needed 20 seconds less than inexperienced workers on the average for installing the rubber stopper. In the case of the metal stopper, 3 persons with VI-work experienced and 5 persons with no experience d in VI-work needed 25.4 seconds and 26.4 seconds, respectively.

      Metal stopper
      3 experienced workers-----25.4 seconds

      5 inexperienced workers-----26.4 seconds

      Unlike the rubber stopper, the average times for installing the metal stopper were almost the same between experienced workers and inexperienced workers. We also carried out a microbiological test for 6 months regarding VIs with the rubber stopper and the metal stopper. The result showed that the insides of all the VIs were kept (negative and) germ-free. Based on the results mentioned above, we concluded that the prototype metal stopper is as useful and practical as the rubber stopper.