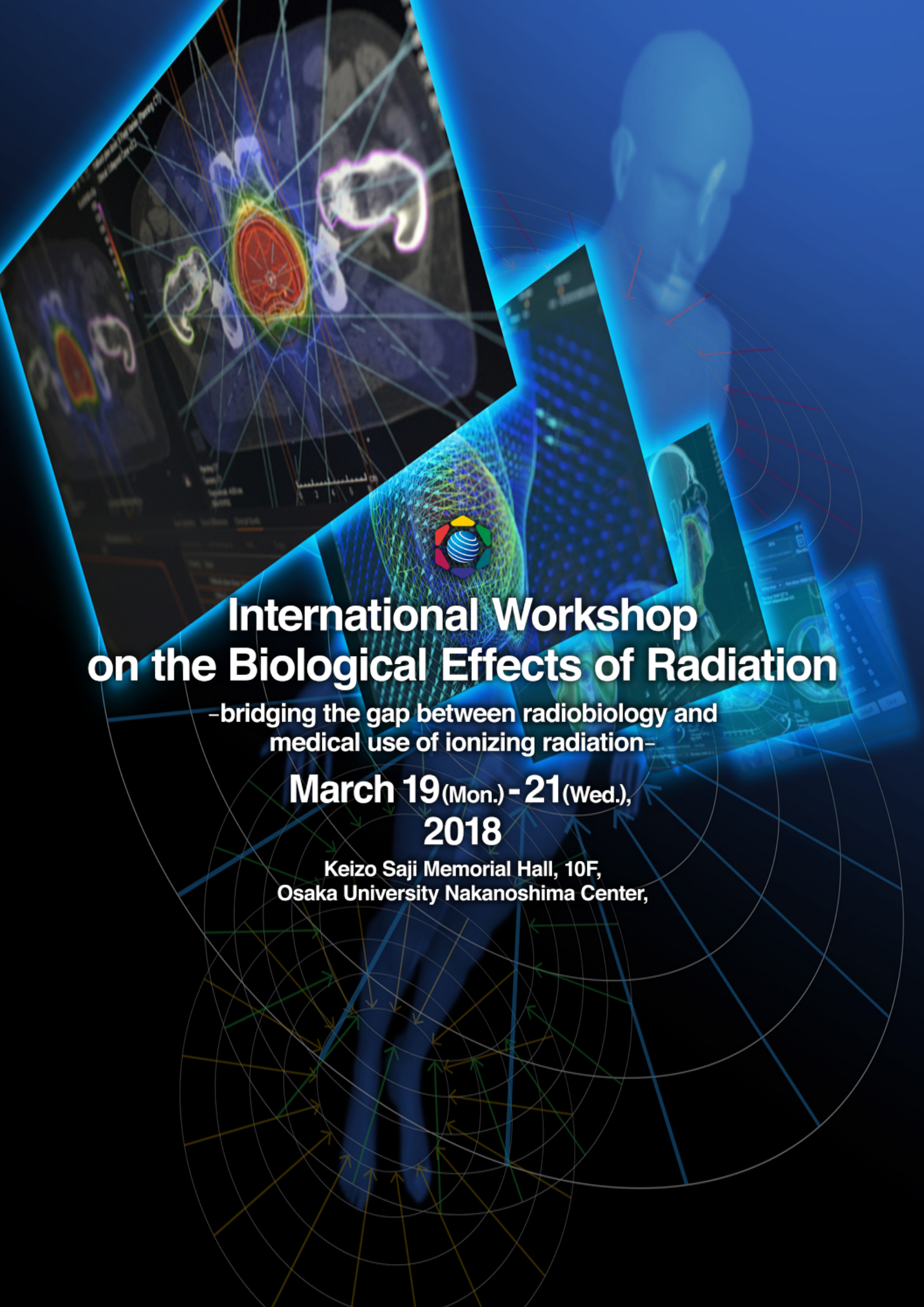

International Workshop on the Biological Effects of Radiation

–bridging the gap between radiobiology and medical use of ionizing radiation–

March 19(Mon.) - 21(Wed.), 2018

Keizo Saji Memorial Hall, 10F,
Osaka University Nakanoshima Center,

International Workshop on the Biological Effects of Radiation

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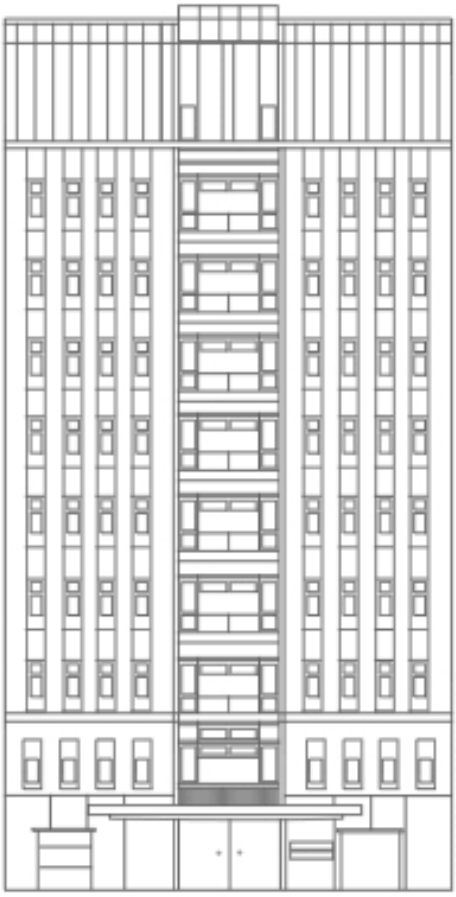

Main site: 10F

Keizo Saji Memorial Hall

Reception (Welcome meeting): 9F

Poster session & coffee : 4F (406)

Osaka University Nakanoshima Center

4-3-53 Nakanoshima, Kita-ku, Osaka 530-0005, Japan

Tel : +81-6-6444-2100

Fax : +81-6-6444-2338

Wireless network for guests

SSID : onc-ap

PASS : oncap178wh8ba

Program

1st day (19th March)

8:45 -	The hall & the reception desk (at 10F lobby) opening
9:30 -	Opening address Dr. Wolfgang Weiss (ex-UNSCEAR Chair) Overview of this workshop Dr. Yoshiharu Yonekura (ex- NIRS President, ex-UNSCEAR Chair)
9:45 - 11:45	Morning session **1.1. Dose and Dose-rate Effects** Chairperson: Dr. Ulrike Kulka (BfS)
1M01	Dose- and Dose-Rate Effects of Ionizing Radiation for Cancer Incidence and Life-Shortening. Dr. Gayle Woloschak (Northwestern University)
1M02	Life span and tumorigenesis in mice exposed to continuous low dose-rate gamma rays. Dr. Ignacia Braga-Tanaka (Institute for Environmental Sciences)
1M03	How high can you go, radionuclide therapy is effective at low dose rate. Dr. Mark Konijnenberg (Erasmus MC)
11:45 - 13:00	Lunch break
13:00 - 15:30	Afternoon session I **1.2. From Mutation to Cancer** Chairperson: Dr. Masako Bando (Kyoto University, Osaka University)
1A11	Overview: The divergence of approaches from molecular biology and macro level. Dr. Masako Bando (Kyoto University, Osaka University)

1A12	Responses to low dose radiation in vivo: DNA damage, aging, and immune regulation. Dr. Yi Wang (CNL)
1A13	Dose-rate effects of lymphocyte chromosome aberrations in chronically irradiated mice after age adjustment. Dr. Kimio Tanaka (Institute for Environmental Sciences)
1A14	WAM model - a dynamic equilibrium model for the dose-rate effect. Dr. Yuichi Tsunoyama (Kyoto University)
	Panel discussion "Overcome the divergence of approaches of molecular biology from macro level."
15:30 - 16:00	Coffee break
16:00 - 18:00	Afternoon session II **1.3. Activities of the Consortium for Medicine, Chemistry and Physics at Osaka University** Chairperson: Dr. Atsushi Shinohara (Osaka University) Opening Dr. Atsushi Shinohara (Graduate School of Science, Osaka Univ.)
16:05 - 16:20 1A21	Medicine and science collaborative research for targeted alpha therapy in Osaka University. Dr. Koichi Fukase (Graduate School of Science, Osaka Univ.)
16:20 - 16:45 1A22	Production and isolation of At-211 for targeted alpha therapy at Osaka University. Dr. Zijian Zhang (Graduate School of Science, Osaka Univ.)
16:45 - 17:10 1A23	Radiolabeling of small molecules with astatine(^{211}At) for theranostics. Dr. Yoshifumi Shirakami (Graduate School of Medicine, Osaka Univ.)
17:10 - 17:35 1A24	Preparation of novel anticancer drugs using At-211. Dr. Kazuya Kabayama (Graduate School of Science, Osaka Univ.)
17:35 - 18:00 1A25	Imaging of the targeted alpha therapy for the clinical application. Dr. Tadashi Watabe (Graduate School of Medicine, Osaka Univ.)

2nd day (20th March)

9:00 - 11:30	Morning session **2.1. Medical Database** Chairperson: Dr. Nobuyuki Osakabe (Hitachi, Ltd.)
2M01	Biomarkers and radiation therapy for patients with head and neck cancer. Dr. Pierre Saintigny (Cancer Research Centre of Lyon)
2M02	Present status of patient dose in large part of the world. Dr. Madan Rehani (MGH, HMS/IAEA)
2M03	Millennial medical record project - Toward establishment of authentic Japanese version EHR and secondary use of medical data – Dr. Hiroyuki Yoshihara (Kyoto University, University of Miyazaki)
	Panel discussion “How can medical database be effectively used in the BER study and practice?” Panelist: Dr. Nobuyuki Osakabe (Hitachi, Ltd.) & all speakers
11:30 - 13:00	Lunch break
13:00 - 15:00	Afternoon session I **2.2. Imaging Techniques for Radiotherapy and Cancer diagnosis** (Big data and diagnosis, treatment) Chairperson: Dr. Jun’ichi Kotoku (Teikyo University)
2A11	Potentials of Radiomics in Cancer Treatment. Dr. Hidetaka Arimura (Kyushu University)
2A12	Imaging database and radiomics. Dr. Akihiro Haga (Tokushima University)
2A13	Radiomics on MRI field. Dr. Koji Sakai (Kyoto Prefectural University of Medicine)

15:00 - 15:30	Coffee break
15:30 - 17:30	Afternoon session II **2.3. Radiation Biology and Medical Use** Chairperson: Dr. Akihiro Haga (Tokushima University)
2A21	Contribution of biological analysis platform to optimize the medical use of ionizing radiation. Dr. Ulrike Kulka (BfS)
2A22	Quantitative personalized oncology - Mathematical models for precision radiotherapy. Dr. Heiko Enderling (Moffitt Cancer Center)
2A23	Medical radiation protection research strategies in Europe and the role of the medical physicist in Europe. Dr. Christoph Hoeschen (Otto-von-Guericke University)
18:00 - 19:30	Poster session Room No.406 (4F)
19:30 - 21:30	Reception (Welcome meeting) Salon (9F)

3rd day (21st March)

9:00 - 11:30	Morning Session **3.1. Presidential Session: International Cooperation in Biological Effects of Radiation** Chairperson: Dr. Yoshiharu Yonekura (ex-UNSCEAR Chair)
3M01	Understanding low dose radiation exposure effects : MELODI's views on developing international cooperation. Dr. Jacques Repussard (MELODI)
3M02	Electric Power Research Institute International Dose Effect Alliance. Dr. Donald A. Cool (EPRI, IDEA)
3M03	Low-Dose Radiobiology Program at Canadian Nuclear Laboratories: Past, Present and Future. Dr. Dmitry Klokov (CNL)
3M04	Planning and Acting Network for Low Dose Radiation Research (PLANET) and promotion for integrated network in Japan. Dr. Yutaka Yamada / Dr. Yoshiya Shimada (QST, PLANET)
3M05	JSPS committee "multidisciplinary research on the biological effects of radiation". Dr. Takahiro Wada (JSPS committee)
	Short talks on each organization / panel discussions
11:30 - 13:00	Lunch break
13:00 - 15:00	Afternoon session I **3.2. Radiation Protection in Medicine** **3.2.1. Radiation induced cancer** Chairperson: Dr. Yoshiya Shimada (QST)

3A11	Radiation protection in therapy with radiopharmaceuticals. Dr. Makoto Hosono (Kindai University)
3A12	Experimental evaluation of the carcinogenic effect of carbon ions and neutrons in children. Dr. Tatsuhiko Imaoka (NIRS, QST)
3A13	Second cancer after radiotherapy. Dr. Jean-Marc Cosset (Amethyst Group, former ICRP C3 member)
15:00 - 15:30	Coffee break
15:30 - 17:30	Afternoon session II **3.2.2. New medical equipment for less radiation dose** Chairperson: Dr. Makoto Hosono (Kindai University)
3A21	Cancer risk from paediatric CT scanning. Dr. Elisabeth Cardis (Institut de Salut Global de Barcelona)
3A22	Low-dose CT screening for lung cancer. Dr. Takeshi Nawa (Hitachi General Hospital)
3A23	Development of low dose diagnostic CT. Dr. Takashi Tanaka (Canon Medical Systems)
17:30 - 17:45	Closing Remarks

Abstracts of Oral Presentations

1M01

Dose- and Dose-Rate Effects of Ionizing Radiation for Cancer Incidence and Life-Shortening

Gayle E Woloschak, Tatjana Paunesku, Ben Haley, Alia Zander

Northwestern University School of Medicine, Chicago IL 60611

Effects of radiation on living organisms are numerous, with significant differences depending on total radiation dose, dose rate etc. Nevertheless, there is a custom in the radiation protection to try to describe all of the radiation effects with a linear non-threshold (LNT) model. The most recent BEIR VII report depended on LNT model was subjected to many subsequent criticisms. For example, in an exchange of opinions between Crowley and others and Calabrese and O'Connor in 2015 (Crowley et al Radiat Res. 2015 Apr;183(4):476-81.) BEIR VII approach to calculation of dose and dose rate effectiveness factor (DDREF) was criticized and the authors showed how different the same collection of data (specifically from table 4 from Preston et al. Radiat Res 2007; 168:1–64) looks when plotted as linear or semi-logarithmic plots. Nevertheless, LNT model is still used for radiation protection. However, despite the use of this model most regulations of worker exposures also place a significant emphasis on limiting possible radiation damage for given time period. For example, astronauts have prescribed maximal monthly, yearly and career exposures (Nelson. Radiat Res. 2016 Apr;185(4):349-58). Thus, radiation protection policies implicitly rely on understanding that biological aspects of radiation risk depend on radiation delivery over time, even though dose protraction is not one of the questions included in the LNT model.

Recent work from our laboratory (Haley et al. PLoS One. 2015 Dec 9;10(12):e0140989; Paunesku et al. Int J Radiat Biol. 2017 Oct;93(10):1056-1063) considered ways in which BEIR VII evaluation of DDREF disregarded much of the animal radiation data and made a direct comparison between animals exposed to protracted or fractionated vs. acute radiation exposures. As shown in Figure 1 (replicated from Paunesku et al. Int J Radiat Biol. 2017 Oct;93(10):1056-1063) a direct comparison of acute and protracted radiation exposures up to 1.5 Gy using linear-liner model has a better goodness of fit than a comparison that uses linear-quadratic model.

It is probable that the focus on LNT model in radiation biology is one of the core problems in low dose research, not so much because this model is flawed, but because the very notion that that type of model may explain effects of radiation is wrong. In essence, all such studies assume that the probability that one cell of a multicellular organism will acquire multiple mutations transforming it into cancer is equivalent to induction of a single lethal chromosomal aberration in a single cell in cell culture. A clear contrast between these two statements should tell us that we are not modeling what should be modelled. Our computational powers are increasing and yet we still insist on testing different types of regression analyses using the data that is clearly too variable to be described by any one single curve.

We propose that is possible to envision new ways of modeling that would synergize with animal research and capitalize on biological variation as the long established and the most fruitful source of all biological knowledge. Just as any wet bench scientist knows that it is not possible to obtain good data without positive and negative controls, new computational approaches can be envisioned that would try to include a portion of the data that is deliberately selected to be “skewed” and where the test data are expected to fall within or outside of certain expected domain. Using animal models one can not only do experiments with positive and negative controls but also try to produce predictive models. “New” modeling of cancer as an outcome of radiation damage could focus on volume of specific type of DNA

damage per cell, the likelihood of engagement of a given DNA repair mechanism or conversely, the likelihood of its failure.

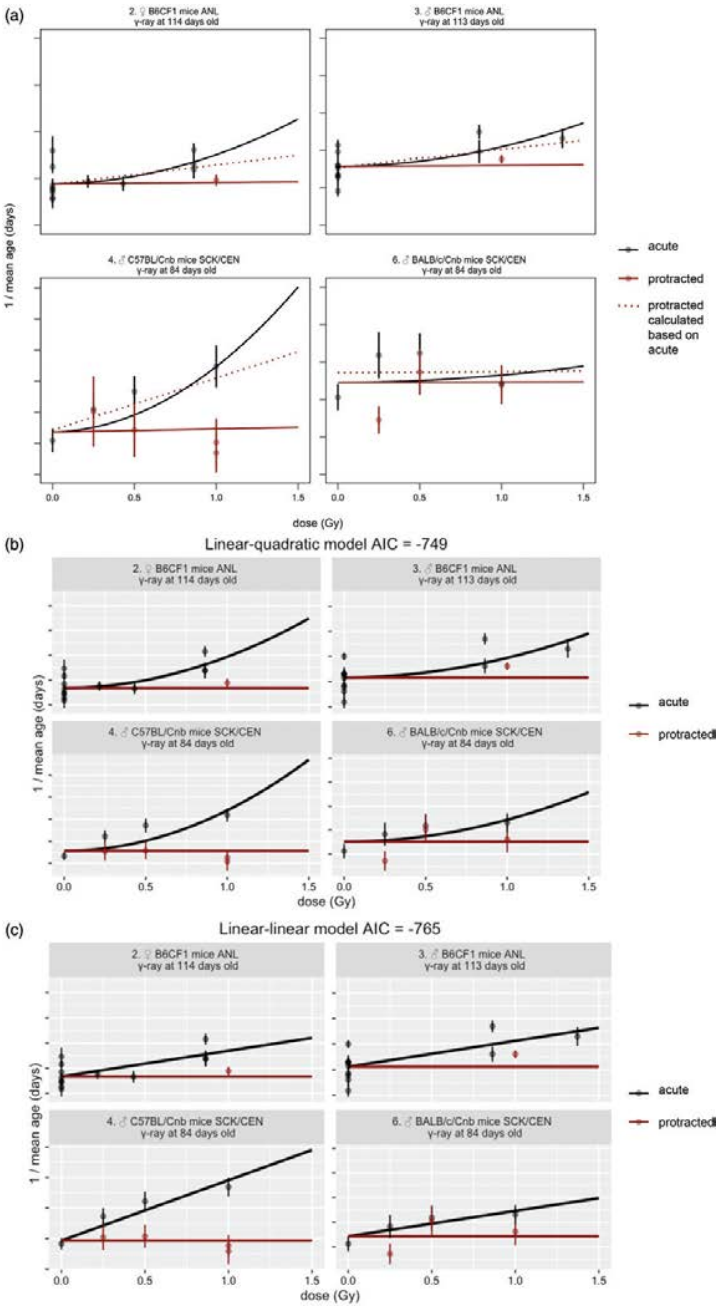

Figure 1. Life-shortening data from mice exposed to acute and protracted radiation up to 1.5 Gy total dose, following BEIR VII procedure (for more details see Haley et al. 2015); currently used model based on linear-quadratic formula and alternative linear-linear model comparisons. Comparison of predicted life-shortening from protracted radiation exposures in a 0–1.5 Gy total dose range when only acute animal irradiation data on life-shortening is used to calculate DDREF (dotted red line) vs. when both acute and protracted data are compared (full lines) (a). In both cases calculations are based on BEIR VII approach, however, in one case (dotted red line) the graph is based on acute exposures, similar to extrapolations done from A-bomb survivor data. In the other case, calculation is done considering both acute and protracted dose exposures; and the graph of life-shortening associated with protracted exposures is shown by a full red line. Moreover, a simpler liner-linear model provides a better fit with the data than the currently used linear-quadratic model. The Akaike Information Criteria (AIC) estimates appear above each fit and quantify the goodness of fit: a lower value indicates a better fit. Overall AIC value for linear-quadratic model (-749) (b) is greater than the AIC value for liner-linear model (-765) (c), indicating that the linear-linear model fits the data (from Paunesku et al. Int J Radiat Biol. 2017 Oct;93(10):1056-1063.).

1M02

Life span and tumorigenesis in mice exposed to continuous low dose-rate gamma rays

Ignacia TANAKA
Department of Radiobiology, Institute for Environmental Sciences

Abstract

Late effects of low-dose and low-dose-rates of ionizing radiation are potential hazards to radiation workers and to the general public, and have become a serious concern in the recent years, and even more so after the Fukushima accident. Our institute has been studying the late effects of continuous low dose-rate radiation exposure in mice for over 20 years.

In 2002, we completed life span study using 4000 male and female 8-week-old specific pathogen free (SPF) B6C3F1 mice. The irradiated groups were exposed to ^{137}Cs gamma rays at dose-rates of 21, 1.1 and 0.05 mGy/day for approximately 400 days with total accumulated doses equivalent to 8000, 400 and 20 mGy, respectively. All mice were kept under SPF conditions until natural death and pathological examination was performed to determine the cause of death. Statistical analyses showed that the life spans of mice of both sexes irradiated with 21 mGy/day (total dose = 8 000 mGy) and of females irradiated with 1.1 mGy/day (total dose = 400 mGy) were significantly shorter than the non-irradiated control group. The life spans, tumor incidence and tumor spectra in mice exposed to 0.05 mGy/day (a total dose of 20 mGy) was not significantly different from the non-irradiated control group. Life shortening was attributed to premature death due to various types of neoplasms including malignant lymphomas. In addition, significant increases in the incidence of hemangiosarcomas, liver, lung, adrenal, ovary and Harderian gland neoplasms were observed in mice exposed to 21 mGy/day. These results suggested that continuous exposure to low-dose-rate gamma-rays for long periods causes either early onset or increased progression of neoplasms.

To clarify whether life shortening was due to shortened tumor latency (early onset) or increased tumor progression, 8 week-old SPF female B6C3F1 mice were exposed to 20 mGy/day for 400 days. On the day 100 of irradiation, 60-90 mice were sacrificed, and every 100 days thereafter up to day 700 (300 days after completion of irradiation), alongside age-matched non-irradiated controls. Pathological examination was performed on all mice to identify lesions, as in the life span study. Completed last year □ results show that increased incidences with no shortening of latency periods for malignant lymphoma, hepatocellular adenomas/carcinomas, bronchiolo-alveolar adenomas and Harderian gland adenomas/adenocarcinomas in irradiated mice. Increased incidence with shortened latencies for adrenal subcapsular cell adenomas, ovarian were observed in the irradiated mice. The results show that continuous exposure to low dose-rate gamma rays in female B6C3F1 mice caused both cancer induction (shortened latency) and promotion/progression (early death), depending on the neoplasm□s organ/tissue of origin.

Recently, we completed the experimental phase of a transgeneration study using C57BL6 males exposed to continuous low dose-rates similar to the life span study. After completion of the 400 day

exposure, the males were bred to non-irradiated 8-week-old virgin C57BL6 females to produce F1 mice. Randomly selected F1 were bred to produce F2. All the mice except the dams of F1 mice were kept until natural death and were subjected to pathological examination. Although there was no significant difference in the pregnancy (F0) and weaning rates (F1) between the irradiated and non-irradiated groups, litters from sires exposed to 20 mGy/day had significantly decreased mean litter size and mean number of pups weaned. Lifespans of sires (F0) exposed to 20 mGy/day and their male progenies (F1) were significantly shorter than the non-irradiated controls. Pathological examination are still in progress.

The studies were performed under contract with the Aomori Prefectural Government, Japan.

How high can you go, radionuclide therapy is effective at low dose rate.

Mark Konijnenberg Dept. Radiology & Nuclear Medicine, Erasmus MC, Rotterdam, Netherlands

Therapy with radionuclides have been very successful in the treatment of various diseases depending on the specific uptake of the radionuclide or vector-drug it is labelled to. Thyroid disorders and metastasized thyroid cancer can be treated with ^{131}I as iodide is taken up by the thyroid follicular cells through the sodium/iodide symporter (NIS) protein. Metastatic neuroendrine tumours (NET) are successfully treated with ^{177}Lu-DOTA-octreotate, with targeting by the somatostatin analog peptide octreotate to somatostatin –receptor expressing lesions. Liver cancer therapy is applied with intra-arterial administration of ^{90}Y and ^{166}Ho labelled microspheres, which get trapped in the small vascular branches around liver tumour lesions. Still experimental, but very promising is ^{177}Lu PSMA for therapy of advanced (metastasized) stage prostate cancer , where PSMA (prostate specific membrane antigen) is the targeting vector as this cell membrane protein is upregulated in prostate cancer.

These radionuclide therapies deliver absorbed doses at a low dose rate according to an exponential decay pattern, determined by both physical decay of the radionuclide and the clearance rate of the radiopharmaceutical. Systemic drug delivery makes that also physiological organs will be taking up radionuclides and irradiated besides the specific uptake in organs and tumour lesions. In peptide receptor radionuclide therapy (PRRT) off target uptake and radiation will occur in the kidneys by physiological clearance of the radiopeptide in the circulation. In the radio-embolisation therapy off-target radiation exposure will occur in healthy liver tissue surrounding the targeted tumour lesions. Radionuclide therapy therefore requires patient-specific dosimetry for treatment planning to obtain safe absorbed doses to normal tissues and efficacious absorbed doses in tumours.

Our department (Erasmus MC, Rotterdam, Netherlands) pioneered development of this therapy and recently finalized phase III clinical trials with a fixed activity administration schedule of 4 x 7.4 GBq,. This trial lead to favourable outcomes (increase of progression-free survival and life quality). Most patients will, however, demonstrate relapse of the disease after PRRT with limited treatment options left. Salvage retreatment with 2 x 7.4 GBq is offered to these patients. Possibly relapse can be prevented by administering higher doses or more cycles of activity to enhance the probability of a complete cure. Simply administering a higher dose will leads to unacceptable healthy tissue damage, especially in the bone marrow (due to circulation) and kidneys (due to clearance and reabsorption) . Response of tissue is not well known at the low to very low dose rates involved (initially in the order of 0.05 - 0.25 Gy/h). Knowledge of the dose-effect curves at very low dose rates is of great importance to design dosimetry guided treatment planning for PRRT.

Repair of sub-lethal damage will occur during the absorbed dose delivery and by this counteract the cytotoxic effects for the radiation. A dose-response curve was found in PRRT with ^{90}Y-DOTA-octreotide for the occurrence of late (> 1 year after the last therapy cycle) toxicity in the kidneys. The absorbed dose to the kidneys did not indicate a correlation with the induction of late renal toxicity, but the Biologically Effective Dose (BED) derived from the Linear-Quadratic (LQ) model did. The absorbed dose limits for PRRT are higher than the known dose-constraints for external beam therapy. This increase is associated with the increased repair of sub-lethal DNA damage during the dose delivery at low dose rate with PRRT. Also spatial heterogeneities in activity and absorbed dose influence the dose response, mainly caused by the specific radiopharmaceutical uptake and the

range of the emitted particles in relation to the distance from decay site to the functional units defining the organ's performance status.

According to the LQ model the BED as a function of time T can be defined as:

$$BEDT=DT+GT\alpha\beta D2(T),$$

with D(T) the absorbed dose and α/β the ratio between the linear and the quadratic radiation sensitivity parameter. BED indicates the exponential relation with the surviving fraction of functioning cells with the factor α. The Lea-Catcheside factor G(T) expresses the accumulation of unrepaired DNA damage into lethal damage combinations during the dose the dose delivery and it is defined as:

$$GT=2D2T0TDt0tDt\prime\varphi t-t\prime dt\prime dt$$

with D(t) the absorbed-dose rate as function of time and φ(t) the repair function in effect during the interval between t' and t and usually assumed to be a single-exponential process with repair half-life T_{rep}, and rate constant μ = $\ln(2)Trep$. If also the dose build-up proceeds according to a single-exponential curve with time and (effective) decay constant λ = $\ln(2)Teff$, G(T) simplifies in the limit T →∞ to: $\lim T\to\infty GT=\lambda\lambda+\mu=TrepTrep+Teff$. In the case of a dose D given in fractionated external beam radiotherapy with fractions of d : $BED=D1+d\alpha\beta.$

BED is commonly used in external-beam radiotherapy and brachytherapy to convert between different fractionation schemes. In radionuclide therapy the relationship between BED and the incidence of renal complications after ^{90}Y-DOTA-octreotide was comparable to that obtained for external-beam radiotherapy. Surprisingly the LQ model seems also to be valid at the very low dose rates in radionuclide therapy. The LQ model parameters are semi-empirically determined for kidneys and liver. For toxicity in other organs at risk after radionuclide therapies as the salivary glands (especially in PSMA therapy) these values are not known.

The LQ model parameters for tumour response after radionuclide exposure are not well known at all. In analogy to high dose rate radiotherapy is the α/β ratio most probably higher than in normal organs. Dose effect curves for tumour response after both ^{90}Y as ^{177}Lu PRRT indicate that doses of > 200 Gy are needed to induce size reduction. Absorbed doses needed by beta-emitters to reduce small (sub clinical) metastatic lesions are not well known. High LET radiation by alpha-particle emitters is considered to optimize therapeutic effects in these small lesions. Preclinical research is performed to determine the possible enhancement by alpha-emitters.

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J Strosberg et al., N Engl J Med 2017;376:125-35
L Strigari et al., Eur J Nucl Med Mol Imaging. 2014;41:1976-88
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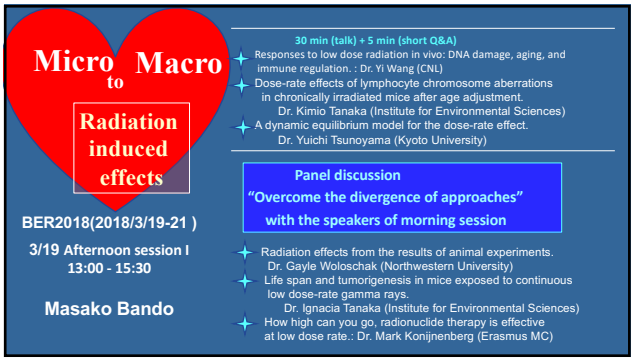
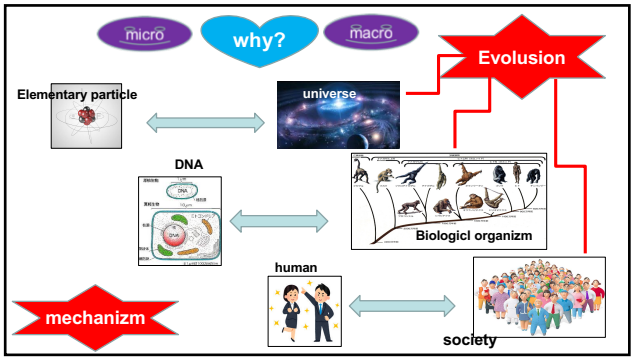
1A11

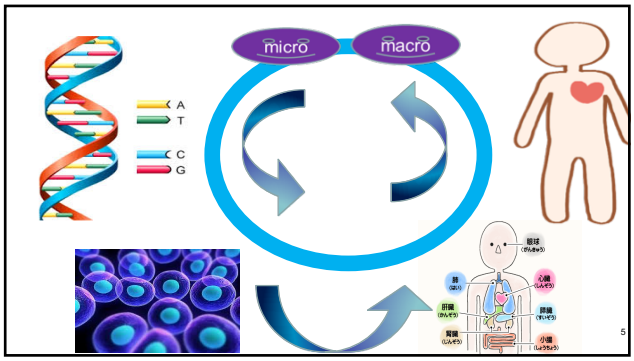
Overview: The divergence of approaches from molecular biology and macro level.

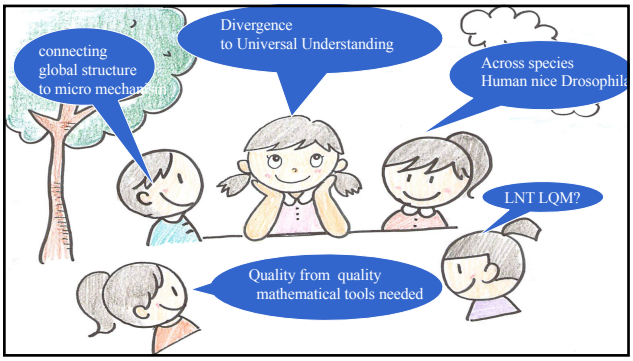
Masako Bando

Yukawa Institute for Theoretical Physics, Kyoto University / Research Center for Nuclear Physics (RCNP), Osaka University









Micro to Macro

③

DNA damage & mutation

7

Radiation

Endogenous

micro

Cell damaged

Mutation

micro

Radiation

Endogenous

ROS

Direct

ROS

Thermal instability

Replication error

Cell damaged

Damage control system

Immune control system

Mutation

Germ cell

Mutation

Somatic cell

animal experiments
Dr. G. Woloschak
Dr. Yi Wang (CNL)
Dr. K. Tanaka
Dr. I. Tanaka
Dr. Yi Wang (CNL)

heredity evolution

Directly observed in F1 or F2

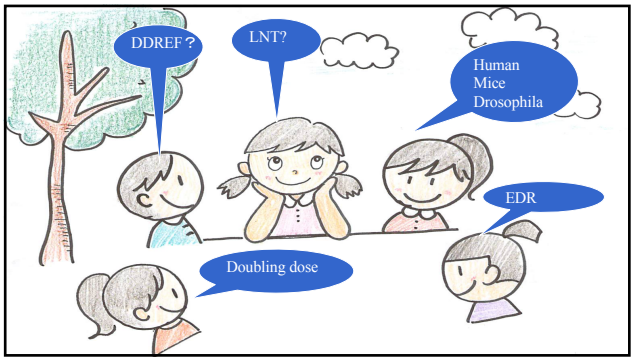
animal experiments
Muller & Russel
Dr. Y. Tsunoyama

?? Complicated many steps with variety of effects

Carcinogenesis initiation

Cancer

Cancer death



Let's have hot interdisciplinary discussions!

12

Responses to low dose radiation in vivo: DNA damage, aging, and immune regulation

Yi Wang*, Youssef Ismail, Dmitry Klokov

Canadian Nuclear Laboratories, Chalk River, Ontario, Canada

Biological and health effects of low doses of radiation (LDR) are extensively studied and debated by both experimental and epidemiological research. The Linear No-Threshold (LNT) hypothesis, assuming that all doses increase the risk of cancer, birth defects, and heritable mutations, is currently used in all radiation protection practices. Although the LNT hypothesis is a simple and convenient method to optimize procedures and regulations in radiation protection, its usage remains controversial. LNT hypothesis is majorly supported by the Atomic Bomb Survivor studies (*1, 2*), however, many recent studies suggest that the responses per unit dose at low doses cannot be predicted by linear extrapolation of responses observed per unit dose at high doses (*3*). Earlier research from our laboratories found that the LDR prolongs the latency of high dose radiation-induced myeloid leukemia in CBA/H mice (*4*). It also increases the latency of spontaneous lymphomas and spinal osteosarcomas (*5*), or high dose radiation-induced cancers in cancer-prone, radiation-sensitive Trp53(+/-) heterozygous mice (*6*). Our data suggest that a single, low, whole body dose (less than 100 mGy) of radiation increases cancer latency and consequently prolongs the lifespan in both wild-type and cancer-prone mice. The results demonstrate that the assumption of a linear increase in risk with increasing dose in vivo is not warranted and LDR actually has beneficial effects (Radiation Hormesis model). However, this systemic radio-adaptive and radio-protective responses remain unexplained mechanistically.

Because the increased genomic instability is a hallmark of cancer (*7*) and loss of function mutations or alteration in DNA repair genes expression are extensively associated with cancer development and progression, we first investigated whether LDR *in vivo* was capable of enhancing DNA double-strand break (DSB) repair in lymphoid tissues of C57Bl/6J mice. Our data demonstrate that *in vivo* LDR did not affect the rate of rejoining of DNA DSBs in splenic and thymic lymphocytes challenged *in vitro* with a high dose of 2 Gy radiation (*8*). The screen of the expression of a panel of 84 DNA repair genes revealed that base and nucleotide excision repair genes such as *APEX2, DDB1,* and *XPD* are predominantly upregulated in response to a challenging 2 Gy irradiation in mice that were pre-exposed to low priming doses of 20 and 100 mGy compared with mice that were exposed to 2 Gy only. Using a DNA repair functional assay, we demonstrated that recognition and repair of 8-oxoG in plasmid DNA, accomplished by base excision repair, is enhanced in nuclear extracts prepared from the spleens of mice irradiated

with low doses and a 2 Gy challenging dose compared with 2 Gy only. Our results indicate that DNA excision repair may be responsible for the suppression of tumorigenesis in LDR induced mice.

Aging has been defined as a progressive decline of organ function, with loss of homeostasis and increasing probability of illness and death (*9*), and accumulation of age-related DNA damage plays a significant role in aging. Much of the evidence relevant to radiation effects on aging and longevity has been obtained for high doses, whereas the effects of LDR on longevity are very limited and inconsistent. We examined the effect of LDR on aging in mice *in vivo* and found that a single dose of gamma-radiation of 100mGy at delivered at 13 months of age significantly reduced the expression of senescence-associated β-galactosidase in the kidney of 26-month old mice. We also studied the effects of LDR on the immune system of aged mice. Our data indicate that, unlike their young counterparts, LDR delivered to aged mice rejuvenates their immune system as demonstrated by the replenishment of the cytokine profile in plasma, the boost of the colony formation and the activation of the signal transduction proteins in hematopoietic stem cells, the increase of DNA damage and the decrease of cell number in blood mononuclear cells. Overall, our results suggest that LDR evokes a spectrum of molecular, cellular and systemic tissue responses *in vivo* to maintain the balance between cell damage and adaptive cell protection. Therefore, radiation hormesis and/or threshold models might be useful in future radiation protection practices.

References

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Dose-Rate Effects of Lymphocyte Chromosome Aberrations in Chronically Irradiated Mice after Age Adjustment

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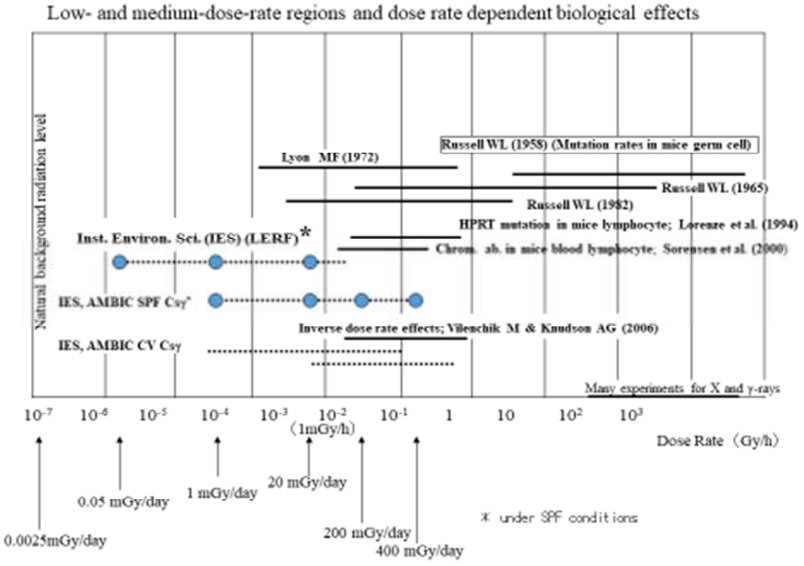
Late effects of very low-dose-rate (LDRs) of ionizing radiation at low-dose range has become serious concern to radiation workers and general public in recent years. However, there is almost no report on the relationship between biological effects and total exposure dose in the chronic exposure at very LDR. So far, many studies have investigated dose and dose-rate effects have been investigated within the LDR and medium-dose-rate (MDR) ranges (Lyon and Morris 1969, Russell and Kelly 1982; Tucker et al. 1998; Sorensen et al. 2000; Ina et al. 2005). LDR and MDR are defined as 6 mGy/h (132 mGy/22h/day) or less and 6 mGy/h-5.94 Gy/h, respectively (UNSCEAR 2010). The Institute for Environmental Sciences (IES) has a unique facility designed to continuously exposed mice under specific pathogen free conditions to ^{137}Cs-gamma rays at three different dose-rates [0.05 mGy/22h/day(0.0023 mGy/h; abbreviated as 0.05 mGy/day hereafter), 1 mGy for 22 h/day (0.045 mGy/h; abbreviated as 1 mGy/day) and 20 mGy for 22 h/day (0.91 mGy/h; abbreviated as 20 mGy/day)], equivalent to photon (γ-ray) levels about 20, 400 and 8000 times higher than natural background radiation, respectively. The dose-rate of 1 mGy/day is corresponding to that of daily dose of cosmetic radiation in space. Lowest dose-rate of 0.05 mGy/day corresponds to that of the annual mean limiting dose for radiation facility workers and also the mean daily air dose measured in the government designated evacuation zone in Fukushima Prefecture after the Fukushima Dai-ichi nuclear power plant accident. The endpoints have included life span, cancer incidence, non-neoplastic disease, genetic effects and oncogene alterations, chromosome aberrations, mutations, gene expression and cellular and tissue responses.

Dose response and dose-rate effects at LDR range of frequencies of chromosome aberrations in spleen lymphocytes in chronically irradiated mice from 56 age at these three different dose-rates were analyzed at each point for up 25 to 700 days, respectively. Non-irradiated age matched control mice were also observed. Spleen lymphocytes were stimulated with ConA, LPS and 4ME and cultured for 46 h to obtain metaphases. Frequencies of chromosome aberrations of dicentrics and translocations detected by

FISH using centromere prove and M-FISH method, respectively, increased almost in linear with irradiation dose in the dose rates of 1 mGy/day and 20 mGy/day, although those of 0.05 mGy/day were not statistically significant. The α coefficient for linear quadratic model ($Y= \beta D^2+\alpha D+c$、 where Y is frequency of chromosome aberrations and D is irradiation dose in mGy) was obtained over a radiation dose-rate range of 1 mGy/day to 20 mGy/day in dicentrics and translocations decreased significantly with reduction of dose-rate, after calculations with adjusting age using multiple linear regression analysis, which is indicating that there is clear dose–rate effects within the LDR range.

The results also indicate that the formula , $1+(\beta/\alpha)D$, for calculation of dose and dose-rate effectiveness (DDREF) based on the DNA repair model recommended by ICRP 1991 is not appropriate. Therefore we obtained DDREF simply as the ratio of HDR (890 mGy/min) to LDR (20 mGy/day) using formula of $(\beta D^2+\alpha_1 D)/\alpha_2 D$. Dose-rate effectiveness (DREF) for dicentrics and translocations at low-dose of 100 mGy were calculated as 4.5 and 2.3, respectively. An attempt to calculate DREF using two parameters for induction of mutations in spleen and liver of *gpt* delta mice exposed to acute and low dose rate (20 mGy/day)(Okudaira et al 2010). Mutations rates of liver as well as spleen of each mouse in the same group including controls were plotted on X-axis for liver and Y-axis for spleen with the same axes scales. After values from age-matched control mice were subtracted, DREF was obtained as 2.43. Organs collaborate each other and such holistic approach will need in future. These studies will be useful for radiation risk assessment and radiation protection. This study was performed under contract with the Aomori Prefectural Government, Japan.



1A14

WAM model - a dynamic equilibrium model for the dose-rate effect

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After the Fukushima Daiichi Nuclear Power Plant disaster, a research group of Japanese theoretical physicists have proposed a mathematical model: WAM (Whack-a-mole) model for expressing increment of mutation frequency depending on dose rates instead of total dose[1, 2]. They are continuing to brush up the model now with biologists, radiation protection experts, medical doctors etc. Here we would like to introduce the outline of this mathematical model and to present the current tasks of this model and those verification results.

1. Whack-a-mole (WAM) model

It is well known that organisms have the potential to repair damaged biomolecules. Although cells suffered damages are deleted or substituted by the various biological mechanisms, rarely damaged cells remain as mutant cells. And also some of mutant cells disappear by mechanisms to eliminate abnormal cells such as cell death. Therefore, it is quite important to consider the balance between occurrence and disappearance of mutant cells in germ stem cells in order to understand the frequency of genetic influence on offspring.
We would like to propose the following formula representing the mutation frequency caused by radiation dependent on its dose rate[1, 2]. This model expresses increase and decrease of the mutant frequency depending on the dose rate as binomial equation in addition to the fluctuation of mutant frequency by spontaneous mutation. We called this formula Whack-A-mole (WAM) model to liken mutation to moles came out of the hole.

$$dF / dt = (a_0 + a_1 d) - (b_0 + b_1 d) F$$

F : mutation frequency d : dose rate
a_0 : spontaneous mutation and those proliferation effect [/hour]
a_1 : mutation by the artificial radiation [/Gy]
b_0 : natural cell death effect [/hour]
b_1 : the effects of cell death by the artificial radiation [/Gy]

2. Comparison of WAM-theoretical values and experimental values in mouse

Russell WL. and his colleagues have been shown that the radiation dose rate effect on mice mutagenesis. Their historical huge amount of experimental data indicated that apparent

difference in the mutation frequency between acute and chronic irradiation[3].

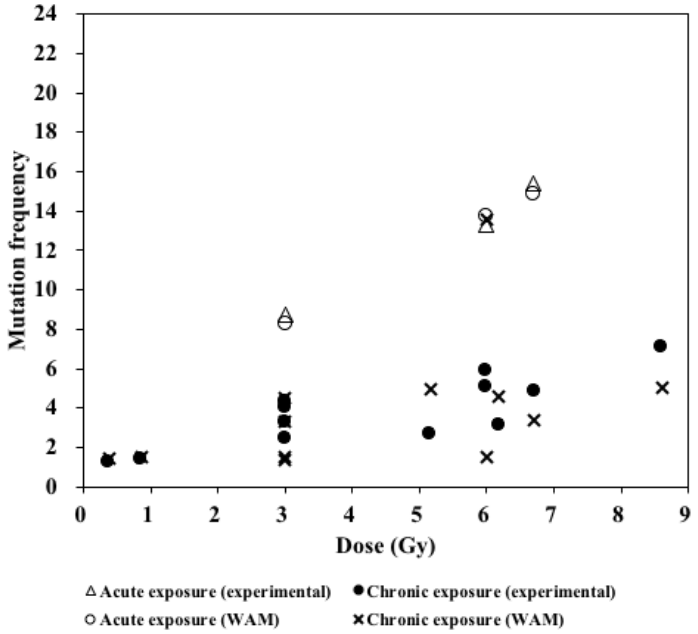

Fig.1

We confirmed that our theoretical values calculated from WAM model agree with the actual values of Russell's experimental results. Although almost WAM theoretical values were clearly well matched with Russell's results which are categorized into two conditions of acute exposure (72 or 90 R/min) and chronic exposure (0.0007 ~ 0.8 R/min), only the value of mutant frequency estimated by WAM model at 0.8 R/min of exposure dose rate apparently excess from its experimental value (Fig.1). It would be possible to summarize in two reasons; 1) Depending on the dose rate, the developmental stage of the irradiated sperm cells was different. 2) The time interval from the end of irradiation to the start of mating is not the same depending on exposure conditions. Currently, we are reviewing their literature and papers[4].

3. Search for ways to overcome barriers between research fields

We have been introducing the WAM model at domestic and international academic societies etc., but unlike physicists, the reaction of biologists was often not so good. I am also a biologist, so the reason can be roughly estimated. It seems to be due to the resistance to expressing the complex system of living organisms by one formula, and also to the weak consciousness against mathematics itself. So, we are currently attempting to create animations that our models can understand intuitively. Our challenge to overcome such barriers between academic disciplines will continue.

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1A22

Production and isolation of At-211 for targeted alpha therapy at Osaka University

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Alpha-particle emitters are promising for the treatment of small tumors because the short recoil range of α-particles emerged from radioisotopes conjugated to appropriate targeting agents is suitable for efficient eradication of cancerous cells with less harmful effects on surrounding healthy organs. Among known α-emitting radionuclides, a limited number of those exhibits suitable nuclear characteristics to the targeted alpha therapy (TAT). One of the potential candidates is astatine-211 (^{211}At) which has preferable properties of a moderate half-life of 7.2 hours and 100% α-decay probability including that of its short-lived electron-capture (EC)-decay daughter ^{211g}Po. At Osaka University, we have recently started the collaborative project for the TAT using ^{211}At. We have been developing large-scale production of ^{211}At, its chemical isolation, radiopharmaceuticals preparation, and clinical trials, all of which are mandated to establish the ^{211}At-TAT. In this contribution, we report the present status of the production of ^{211}At at Research Center of Nuclear Physics (RCNP) and its chemical isolation at Radioisotope Research Center (RRC).

Astatine-211 was produced in the ^{209}Bi(α, 2n)^{211}At reaction at RCNP. A metallic Bi target of 10-30 mg/cm^2 thickness was prepared on 10 μm-thick Al foil by vacuum evaporation. Typical beam current of ^{4}He^{2+} ions was 0.5 particle μA. The Bi target was set at 45^o to the beam axis in an irradiation chamber. The 30-MeV α-beam delivered from the AVF cyclotron passed through a HAVAR window, He cooling gas, 10 μm-thick Al cover foil, and then entered the Bi target with the incident energy of 28.2 MeV. Because the neighboring radioisotope ^{210}At decays into a highly toxic ^{210}Po via an EC decay, the beam energy was adjusted to provide the incident energy on the target lower than 28.6 MeV, which is the threshold energy of the ^{209}Bi(α, 3*n*)^{210}At reaction, to avoid simultaneous synthesis of ^{210}At. During the irradiation, the Bi target was cooled with a circulating He-gas flow and circulating water. Irradiation time was 30 min to a few hours depending on required radioactivity of ^{211}At.

After the irradiation, dry distillation was carried out at RRC to separate ^{211}At from the

target materials. We fabricated a simplified dry-distillation apparatus. In a typical procedure, mixed helium and oxygen gas was used as carrier and reactive gas at a flow rate of 20 mL/min. We also controlled a moisture content in the distillation system. The irradiated Bi target was placed in a quartz still and was heated up to 840^{o}C using an electric tubular furnace. The exit of the quart column was connected to a 4-way valve and then Teflon tube which was cooled with ice water to trap volatile astatine species. During accumulation of ^{211}At on the trap, an X-ray of Po attributed to ^{211}At was measured with a CdTeZn detector to monitor an trapped amount of ^{211}At. After several tens of minutes, trapped ^{211}At was stripped with 100 μL of a desired eluent such as distilled water, saline, or methanol, at a flow rate of 250 μL/min. The radioactivity of ^{211}At was determined by γ-ray spectrometry using a Ge detector. The ^{211}At solution were supplied to pharmaceutical experiments, animal examinations, or our chemical analysis experiments.

At present, after our optimization of the irradiation system, we can produce ^{211}At at the rate of 13 MBq/μA h using a thin Bi target. This means that production capability of our system is 23 MBq/μA h with a thick 40 mg/cm^2 target, which is comparable to the IAEA-recommended value of 25.3 MBq/μA h [1]. Chemical yield of ^{211}At obtained with the 100 μL effluent in the dry-distillation was 80-90% under the optimum conditions. The separation time was typically 60 min. In the workshop, results on our chemical analysis such as ICP-MS measurement on the sample will be also presented.

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Radiolabeling of small molecules with astatine (^{211}At) for theranostics

Yoshifumi Shirakami (Graduate School of Medicine, Osaka University)

Background:

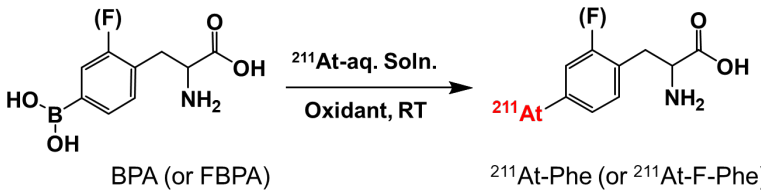
Astatine (^{211}At, $T_{1/2}$=7.2hr) is an alpha particle emitter which is known as the promising radionuclide for nuclear medicine therapy. Furthermore, ^{211}At allows SPECT imaging since the daughter nuclide of ^{211}At, polonium (^{211}Po, $T_{1/2}$=5sec), emits X-rays (77 and 79 keV). Thus, ^{211}At and its labeled compounds are considered to be useful not only for therapeutics but also for diagnostics (theranostics). No ^{211}At labeled agents were launched yet in the world at present. A clinical trial of ^{211}At labeled BC8-B10 was initiated in the U.S. as the world's first clinical trial of ^{211}At labeled agents in 2017 (Phase 1/2 for leukemia, NCT03128034). While the chemical properties of astatine have not been well elucidated since there are no stable isotopes of astatine, which make difficult or slow the development of ^{211}At labeled agents. This article describes the chemistry of ^{211}At aiming to develop sodium astatide (^{211}At) as a potential agent for thyroid cancer and also explains methods for radioastatination of small molecules.

Sodium astatide (Na^{211}At):

Sodium astatide (Na^{211}At) has been investigated for treatment of thyroid cancer as an alternative to sodium iodide (Na^{131}I) which is currently used in a clinical setting. It is well known that Na^{211}At is accumulated in tumors expressing sodium iodide symporters (NIS) as well as in normal thyroid in small animals. Several papers pointed out that the thyroid uptake of Na^{211}At is lower than that of Na^{131}I (3 to 20 times, vary by paper) [1]. The reason of lower accumulation of astatide in thyroid is not well understood. Astatide anion might not be able to couple to thyroxine (a hormone of thyroid), unlike iodide anions, since the ionic radius of astatide (2.3Å) is a little larger than that of iodide (2.16Å). Astatine-211 is produced by a nuclear reaction of ^{209}Bi(α,2n)^{211}At. The produced ^{211}At is separated and purified by a dry distillation method or a wet solvent extraction method and obtained as an aqueous solution in a cold trap. It is assumed that, in contrast to iodine, astatine prefer to present as higher oxidation states, such as At[+1] and At[0], in addition to At[-1] in the aqueous solution. We tried to prepare an aqueous solution of pure Na^{211}At using reducing agents. Ascorbic acid was one of the best agents for reducing the higher oxidation states of At-species into astatide anions. The radiochemical yield of Na^{211}At with 1% ascorbic acid was more than 90%. The solution of Na^{211}At with 1% ascorbic acid showed 3 to 5-times greater thyroid uptake in rats and mice comparing with the solution without ascorbic acid. This result demonstrated that the oxidation states of ^{211}At affects pharmacokinetics of ^{211}At labeled compounds as well as chemical properties of them.

Astatination of small molecules:

Trialkylstannylated precursors can be used for preparation of astatinated molecules as well as for preparation of iodinated molecules since the chemical properties of both astatine and iodine are alike [2]. The astatination reactions often require organic solvents and complicated procedures for heating, deprotection and purification. The residual precursors including tin and by-products in the reaction mixtures should be eliminated from final drug products. We attempted to develop a new method for astatination of phenylalanine (Phe) by substitution reaction of a borono-group in a precursor molecule (Fig.1). Boronophenylalanine (BPA) or 2-fluoro-boronophenylalanine (FBPA) was reacted with ^{211}At-aqueos solution (1-10MBq) in the presence of *N*-bromosuccinimide as an oxidant at room temperature for 30min. Radiochemical yields of ^{211}At-(F)-Phe were more than 90%. The products were stable in the aqueous solution at pH8.5 for 24hr. The borono-substitution reaction is applicable for the astatination of the other arylboronates.



BPA (or FBPA) ^{211}At-Phe (or ^{211}At-F-Phe)

Fig. 1 Astatination of phenylalanine analogue by substitution reaction of borono group in precursor molecule

Future aspects:

Our goals of the studies are to prepare and supply ^{211}At labeled agents for theranostics. Both Na^{211}At and ^{211}At-(F)-Phe analogues will be the potential candidates. We need careful about the designs of molecular structures and formulations of the drug products due to some limitations of astatine from the chemical point of view as follows: 1) Astatine presents as various oxidation states from +7 to -1 resulting in complicated properties for labeling, 2) The energy of covalent bonding between astatine and carbon atoms are relatively weak. It is crucial to ensure the stability of ^{211}At labeled agents both in vitro and in vivo.

This work was supported by JSPS KAKENHI Grant number T16K102770.

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1A24

Preparation of novel anticancer drugs using At-211

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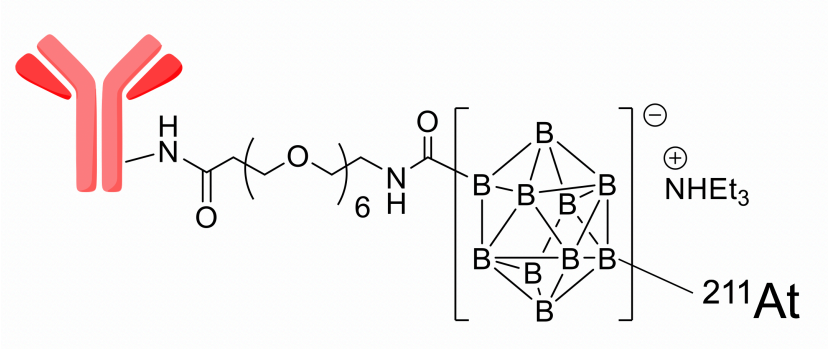
The principal aim of this study was development of next-generation internal radiotherapy using ^{211}At conjugated with cancer targeting molecules.

First, we synthesized anti-CD20 antibody conjugated decaborane ($B_{10}H_{14}$) with polyethylene glycol linker[1-5]. ^{211}At was produced by the cyclotron, and then quickly purified and combined to decaborane conjugated antibody. Now we are getting this ^{211}At combined antibody in about 80% yield.

Next, we performed cytotoxicity evaluation of ^{211}At and this antibody using Raji cells (B lymphocyte cell line derived with Burkitt's Lymphoma). As a result, the time- and concentration-dependent cell death were confirmed in both ^{211}At and this antibody. In the immediate future, we plan to examine that the same study with anti-HER2 antibody for breast cancer, and *in vivo* study using some tumor-bearing animals.



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1A25

Imaging of the targeted alpha therapy for the clinical application

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Targeted alpha therapy is receiving much attention in the field of theranostics because of its high biological effect to the target cancer cells. However, physiological uptakes in non-targeted organs are also observed in the targeted alpha therapy as well as beta-particle therapy, which might lead to the severe side effects. We should consider about both maximizing the treatment effect in the tumor and minimizing the side effects in the organs at risk. In the current clinical protocol of radium-223 for bone metastasis of the castration resistant prostate cancer, injected dose is decided by the body weight of the patient. To achieve dose optimization in the targeted alpha therapy, personalized dosimetry is an ideal method by acquiring the whole body distribution in the first therapy as well as estimating the distribution of the target compound by pre-treatment PET or SPECT. In astatine-211, whole body distribution can be visualized and quantitatively evaluated by gamma-camera imaging with targeting the x-ray which is emitted from the daughter nuclide (polonium-211). These imaging data can be used for the dose optimization for the second targeted alpha therapy. In this talk, I would like to introduce the recent achievements of our preclinical research using astatine-211 and the importance of imaging in the targeted alpha therapy for the future clinical application.

2M01

Biomarkers and radiation therapy for patients with head and neck cancer

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Background: Radiotherapy for head and neck squamous cell carcinomas (HNSCC) is associated with a substantial morbidity and inconsistent efficacy. Human papillomavirus (HPV)-positive status is recognized as a marker of increased radiosensitivity. We have recently proposed an approach for the identification of molecular markers associated with benefit to radiotherapy in patients with HPV-negative disease. Methods: Gene expression profiles from public repositories were downloaded for data mining. Training sets included 421 HPV-negative HNSCC tumors from The Cancer Genome Atlas (TCGA) and 32 HNSCC cell lines with available radiosensitivity data (GSE79368). A radioresistance (RadR) score was computed using the single sample Gene Set Enrichment Analysis tool. The validation sets included two panels of cell lines (NCI-60 and GSE21644) and HPV-negative HNSCC tumor datasets, including 44 (GSE6631), 82 (GSE39366), and 179 (GSE65858) patients, respectively. We finally performed an integrated analysis of the RadR score with known recurrent genomic alterations in HNSCC, patterns of protein expression, biological hallmarks, and patterns of drug sensitivity using TCGA and the E-MTAB-3610 dataset (659 pancancer cell lines, 140 drugs). Results: We identified 13 genes differentially expressed between tumor and normal head and neck mucosa that were associated with radioresistance in vitro and in patients. The 13-gene expression-based RadR score was associated with recurrence in patients treated with surgery and adjuvant radiotherapy but not with surgery alone. It was significantly different among different molecular subtypes of HPV-negative HNSCC and was significantly lower in the "atypical" molecular subtype. An integrated analysis of RadR score with genomic alterations, protein expression, biological hallmarks and patterns of drug sensitivity showed a significant association with CCND1 amplification, fibronectin expression, seven hallmarks (including epithelial-to-mesenchymal transition and unfolded protein response), and increased sensitivity to elesclomol, an HSP90 inhibitor. Conclusion: Our study highlights the clinical relevance of the molecular classification of HNSCC and the RadR score to refine radiation strategies in HPV-negative disease. In our talk, we will summarize few other studies that have proposed biomarkers of response or resistance to radiation therapy in head and neck cancer.

2M02

Present status of patient dose in large part of the world

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The issue of patient radiation dose has been receiving increasing attention globally. Traditionally, when one talks about patient doses on a global scale, one is used to talking about either a) collective effective dose to the population and United Nations Scientific Committee on Effects of Atomic Radiation (UNCEAR) provides data on this or b) per procedure patient dose in different imaging modalities and associated values of diagnostic reference levels (DRLs). But for correlating patient dose with biological effects, one needs to talk about cumulative effective dose to individual patients. Unfortunately, this aspect has not received the attention that it should. In the past, tools to estimate cumulative dose were not available but currently many countries have the technology to track patient exposure history. Besides technology, one needs to use patient identifier (ID) that is valid for life and is used in medical records. Having a network of picture archiving and communication system (PACS) that connects many hospitals in the region of the country or national network and using the same patient ID has enabled tracking of patient doses. Additionally, several commercial vendors are providing dose management systems that provide extensive information on tracking of doses.

The key points in tracking of patient dose with relevance to biological effects are a) assessment of cumulative effective dose and cumulative organ doses to the individual patient and b) estimate of doses for assessing the potential for tissue reactions. Currently, there is data available from imaging studies on thousands of patients who have received radiation dose in the range of 100 to 1100 mSv of effective dose or 100 to 3000 mGy to some of the important organs like breast, heart, lungs, bone marrow, eye, brain, esophagus or colon. We have segregated patients in the category of malignant and non-malignant and in different age groups: 0-30; 31-50 and over 50 years. Although the majority of the patients with higher doses are in upper age groups of >50 and have malignant conditions, there are 1-5% situations where patients are in lower age group (0-30 years) and also those who have non-malignant disease. The data on the frequency of use of relatively high dose examinations, in particular, computed tomography is reasonably available from many countries. The overexposures and accidental exposures are not that common but cases of skin injuries in patients undergoing continue to happen. Regulatory requirements in USA to bring all cases of patients undergoing fluoroscopic procedures with reference air kerma dose exceeding 2Gy and 5Gy to the attention of Radiation Safety Committee of the institute have created data on frequency of such cases. Data on temporal change in frequency and doses is scant but scattered information is available from some studies that indicate positive trends in patient doses. Currently, there is much more availability of patient dose information from developed countries of the world primarily because of commercial availability of dose tracking systems.

The radiation exposure of patients provides a valuable opportunity for using patient population for research on biological effects. Better availability of patient dose indices currently adds higher level of confidence in dose estimates and thus better correlation with radiation effects.

2M03

Millennial medical record project

— Toward establishment of authentic Japanese version EHR and secondary use of medical data —

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Kyoto University, University of Miyazaki

The beginning of EHR can be traced back to the examination of the medical information common standard in 1995 (MML: Medical Markup Language [1]). In 2001, EHR with database structure of MML was developed and expanded to Miyazaki, Kumamoto, Tokyo, Kyoto (Dolphin Project)[2, 3, 4]. After that, the necessity of medical information management at national level and the importance of secondary use of medical information came to be recognized. In 2015 the country level version of the Dolphin Project "The Millennium Medical Record Project" began. We will increase the number of connected hospitals in 4 years until 2018 and prepare for secondary use of medical information starting from 2019. We are aiming for independent profit including EHR department by revenue of secondary use of data without relying on government subsidies.

In the first fiscal year (FY 2015), establish the foundation of the EHR center (database etc). At the same time, we connected hospitals (11 facilities) already connected to the former EHR in Kyoto and Miyazaki to the center.
In fiscal 2016, the number of connected hospitals is increased, 23 hospitals are newly connected, and in fiscal 2017 more than 40 hospitals are scheduled to be connected and adjustment is continuing. In FY 2018, which is the final year of the AMED research period, more than 40 hospitals, pharmacies, etc. are planned to be connected (Fig. 1). The final goal is about 150 in the basic hospital class.

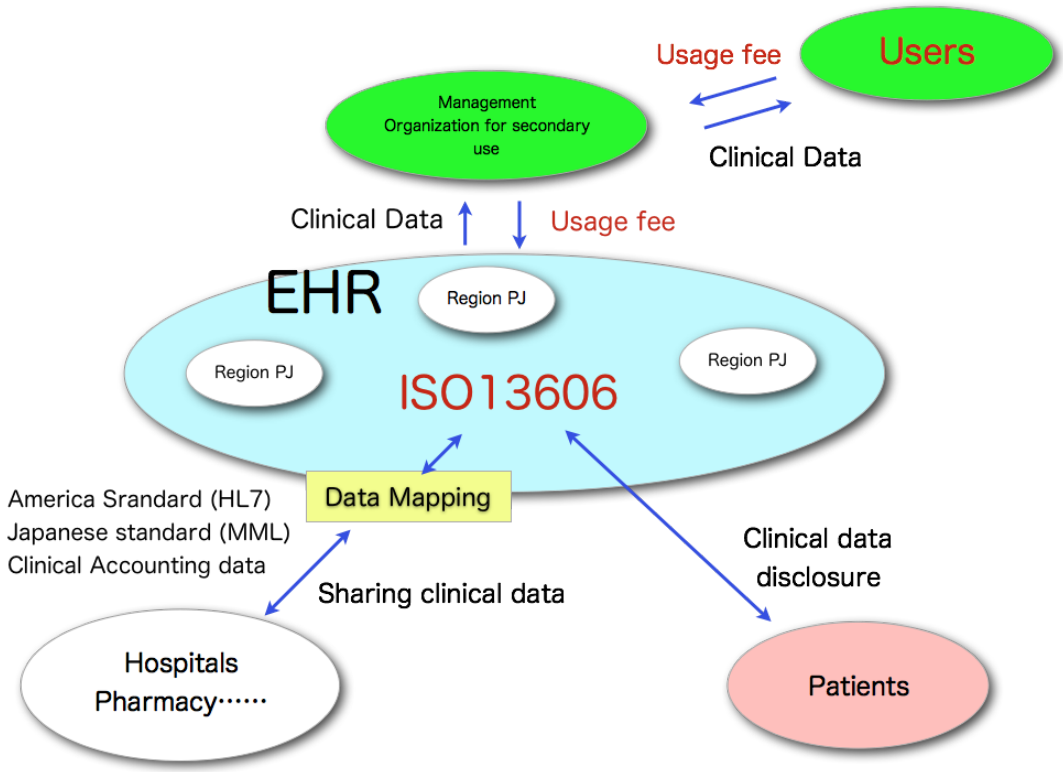

Figure 1. Concept of Millennial medical record. Make large-scale data centers in Japan, accommodate data centers in each region, reduce costs, and reduce operational burden rather than data center operation by region.

As shown in Figure 2, in the Millennium Medical Record Project, we will first build the EHR system in the lower part of the figure (~ 2018) and precede the EHR service. With the enforcement of the Next-Generation Medical Infrastructure Law, two newly established entities (Primary Use EHR Management Organization, Secondary Use Certification Anonymous Processing Medical Information Creation Business Operator) will be operated.

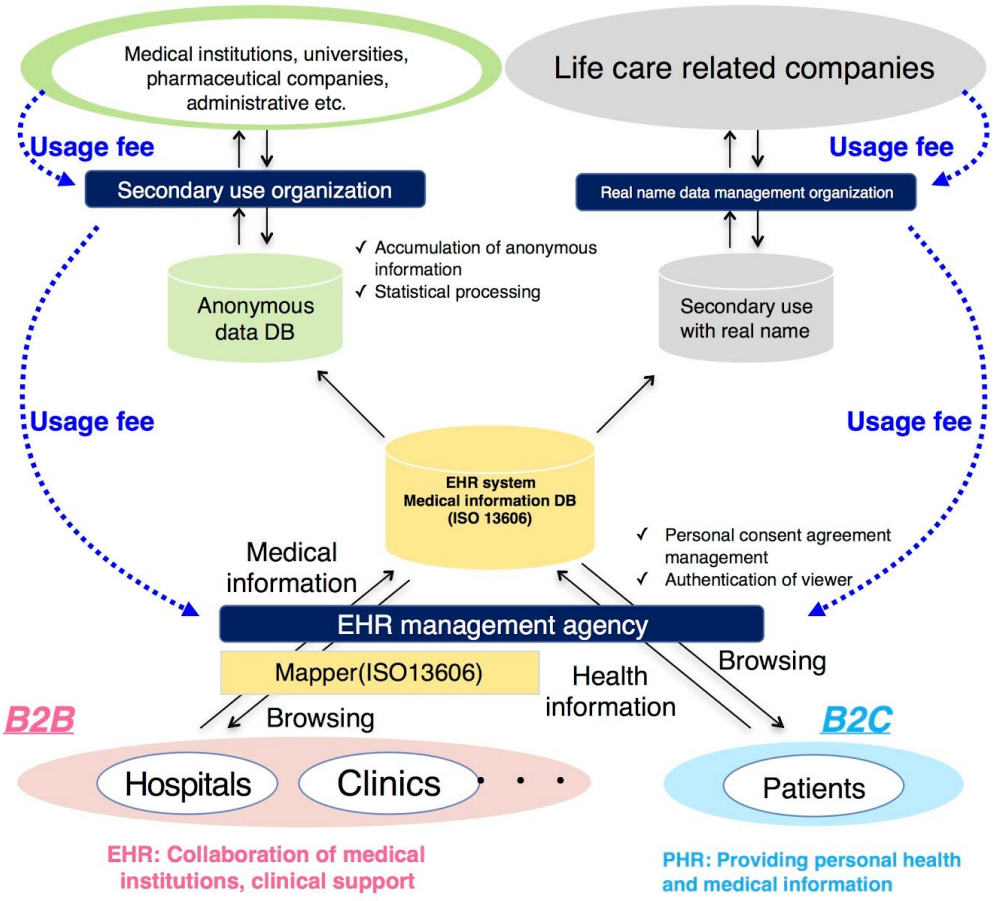

Figure 2 Outline of the Millennium Medical Record Project

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2A11

Potentials of Radiomics in Cancer Treatment

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The radiomics is a novel field, which comprehensively analyzes a large number of medical images, and extracts useful information that can make it possible to improve the decision supports in the cancer treatment including surgery, radiation therapy, and chemotherapy. The radiomics is a word derived from "radio", which means radiological images (medical images in a broad sense), and omics. Omics consists of several study fields (genomics, transcriptomics, proteomics, and metabolomics) that improve our understanding of tumor biology and clinical management of cancer by comprehensively analyzing genome, transcriptome, proteome, and metabolome. The medical images, which are routinely and quickly acquired with low-cost in clinical practices, represent the internal "phenotypic" information (e.g. anatomical, physiological, and pathological information) on tumor regions and patients' bodies. The phenotypes result from the expression of an organism's genetic codes, i.e., genotypes, as well as the influence of environmental factors and the genotype-phenotype interactions. The genotypes with mutations could determine cancer traits, which are involved in the prognoses of patients. On the other hand, the genotypes are assumed to be encoded to the phenotypes expressed in the medical images by biological processes, and then the radiomic features may be computed by "decoding" the phenotypes (medical images). "Decoding" medical images indicates the extraction of image features from medical images using computational image processing and analysis techniques. Therefore, the radiomic features might be equivalent to the genotypes, and thus they could have associations with the cancer prognoses. In conclusion, radiomic features could be considered to reflect cancer traits and prognoses.

Since the radiomic features could have potentials to be employed as "imaging biomarkers" for decision-making in cancer treatment from the assumption mentioned above, the prognoses of patients or treatment outcomes could be predicted by using the features. The author will explain the potentials of radiomics and its perspectives in cancer treatment.

2A12

Imaging database and radiomics

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Radiomics can provide characteristics of entire tumors and of spatial and temporal intratumoral heterogeneity with noninvasive and repeatable way [1]. Radiomics converts medical imaging data into a high-dimensional feature space using a large number of automatically extracted data characterization algorithms. A schematic illustration of the representative process of extracting radiomics features is shown in Fig. 1. Extracted features may be related with the outcome of tumor phenotype, treatment response, and differentiate benign and malignant tumors. Radiomics have drawn an interest due to their possibility of uncovering tumor characteristics that may have otherwise failed to be appreciated by the naked eye.

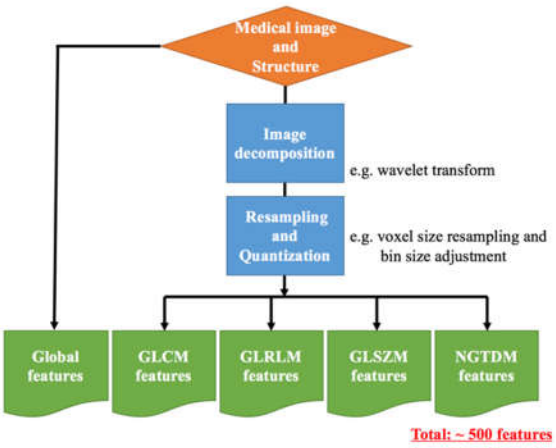

Fig. 1: Representative process in radiomics. As well as the shape and size based features (Global), texture based features are extracted (GLCM, GLRLM, GLSZM, and NGTDM). For extraction of texture features, pre-processing is necessary, which involved isotropic resampling and gray-level quantization.

On the other hand, there are several problems to be overcome in order to improve the radiomics prognosis of the outcome. One is that the radiomics signature has been sensitive to the delineation of the volume of interest (VOI) [2], which is commonly subject to interobserver delineation variability. Second is a variation in medical images used in the radiomics analysis, that is, regarding image quantification or normalization. Third is a limited accessibility to the medical database. Above problems relate each other having inherent difficulties.

In this talk, I'll show the application of radiomics for predicting the histology of early-stage non-small-cell lung cancer (NSCLC) by analysing CT images with interobserver variability for tumor delineation in The University of Tokyo Hospital. Radiomics features are extracted from four VOI delineated independently, and

area-under-the-curve (AUC) analysis is performed. It will be showed that inter-observer variability in delineation is a significant factor in radiomics performance.

One of the limitations of above study is the small cohort size, only 40 NSCLC patients. For extended database, one needs to take carefully image quantification into account. I'll present other validation results by using the Cancer Imaging Archive [TCIA, http://www.cancerimagingarchive.net/], which implies that the quantitative imaging technique is essential in further development of radiomics.

In quantitative CT imaging, the electron density estimation is the easiest way. On the other hand, a diversity of medical imaging devices makes a novel image reconstruction possible. In this talk, I also present the material decomposition approach and functional imaging approach for an application in radiomics. In these approaches, an establishment of imaging database would be a crucial key, too.

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2A13

Radiomics on MRI field

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Literally “Radiomics” is a synthesized word that is derived from radiology and omics. The meaning of omics is the science that systematically integrates wide information in one field. The definition of radiomics reminds us “inter-disciplinarily work” and requires an interdisciplinary collaboration.

In the real world, the main purpose of actual research of radiomics is to precisely explain the role of radiology such as, image diagnosis, decision making of therapy, treatment direction, prognosis, follow-up, and to estimate the harmful effects of radiotherapy by effectively integrate the information obtained from radiological examinations (MRI, CT, PET, SPECT)[1].

The concept of radiomics is widely acceptable to medical field with the limited evidence of application and many ongoing studies. Therefore, the relationships among the elements in radiomics are not well defined and have a potential to investigate new relationship to others.

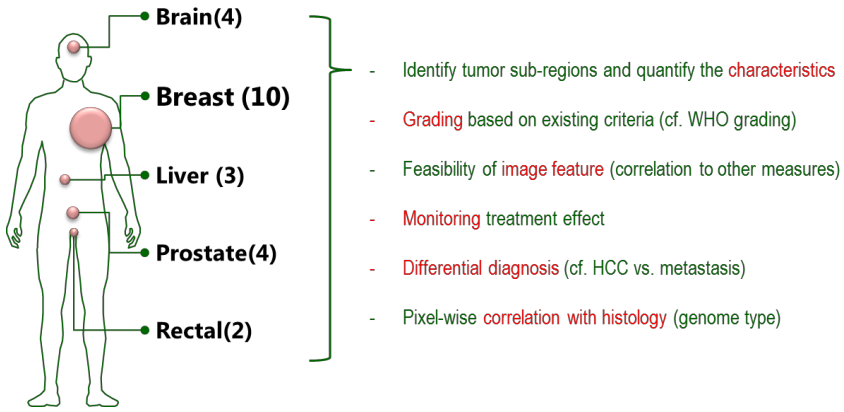
It is possible that we can denote “Radiomics” as the advertisement board of the inter-disciplinarily work from the aspect of radiology. The progress of radiomics may clearly define the position of radiology as “the center of collaboration”. Therefore, radiology can play the role of hub and strong function to further realize the meaning of inter-disciplinarily works.

Research on computer aided diagnosis (CAD) in information science and biomedical science has been studied and made important role to establish basic techniques such as segmentation and registration[2]. As a prominent example, automated tumor extraction and size detection on pulmonary CT has been continued.

The combination of CAD techniques with medical records, which include images, the analyzed data of genes, proteins, and metabolites, and machine learning has created a new paradigm of radiological research. The address of Radiological Society of North America (RSNA) President in 2015 where the key word “Radiogenomics” took special attention as a trend of radiology field. Consequently, some clinical applications of artificial intelligence (AI) came up to the gallery in RSNA 2016.

I believe that the real face of “Radiomics” is a sign-board of radiology centered on integrating multi-disciplinary collaboration and creation of new omics by radiology. It should be noted that this is not only simple summation of each research field (mixing) but integration of multi-disciplinary field. Therefore, it is not “Radio-mix” but “Radiomics”.

The purpose of MRI radiomics on top five body parts were summarized as following figure (as of August 25, 2017).



Those were characterizing, grading of tumor, and investigating image feature, monitoring, information for differential diagnosis, and correlation to histology. The top five MRI radiomics studies were carried out on brain[3,4], breast[5,6], liver[7,8], prostate[9,10], and rectal[11]. On the top 5 body parts, the main target can be summarized as malignant tumor.

Through the review, many papers pointed out the problems of their study as follows: Small cohort size, Retrospective nature, Selection bias, Manual lesion segmentation is operator-dependent, and Very small lesions. Almost of all papers pointed out the “small cohort size” was a big problem. It is easily understand that there is a limit to earn the cohort size at one site.

In my talk, I will review some MRI based radiomics studies. I will also try to categorize the study design and show the stats of radiomics studies in the International Society in Magnetic Resonance in Medicine (ISMRM2017) and its two official magazines, Journal of Magnetic Resonance Image and Magnetic Resonance in Medicine. In addition, I will try to describe the current status of MRI based radiomics.

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2A21

Contribution of a biological analysis platform to support the medical management of radiation accident victims

Ulrike Kulka, BfS

An indispensable element of managing a radiation emergency is reconstruction of the personal, absorbed dose. This will not only help in selecting the optimal treatment, but will also provide the emergency victim with confidence that he/she is properly diagnosed. The latter factor is particularly important following large-scale radiation emergencies, where many people will not know whether they have been exposed or not (the so called worried well). In such cases, retrospective personal dosimetry can provide immense help and to this end a European Network of biological and retrospective physical dosimetry was established, comprising 26 organisations from 16 European countries. Among them are research organisations, universities, hospitals, regulators and radiation protection authorities. Together they provide competences in various fields for emergency preparedness, for radiation research and for radiation protection of patients and personnel. This configuration assures access to laboratories with expert knowledge in different biological assays and physical techniques for individualised dose assessment.

The initial point of the network was to focus on emergency preparedness and response in large-scale radiological incidents by enabling individualised retrospective dose assessment for possibly exposed people, first responders, but also for distressed “worried well” individuals. In such situation, the concerted action of the network partners can help to rebuild trust and prevent a confidence crisis in the affected population groups. Beyond that, the knowledge of the actual received dose is of high importance for the optimal medical care of the actually exposed people. However it has turned out that the network can also contribute to radiation protection in general, including the application of ionising radiation in radiation therapy and nuclear medicine units in hospitals. This will be done by providing an analysis platform to enable individualized approaches, also for smaller or remote hospitals, enabling individualised approaches in medical treatment of patients, e.g. by taking into consideration the individual radiation sensitivity.

Thus, the network with its ready-to-use operational basis, quality assurance and education & training plans, is of benefit for emergency preparedness and response as well as for occupational and medical radiation protection. Even though RENEB is a European network, successful collaborations have been initiated with colleagues from all over the world and links to global institutions as WHO and IAEA have been established.

Most of the network partners are also involved in radiation research and are members of the European radiation protection platforms MELODI, EURAMED, EURADOS, NERIS and ALLIANCE. Now, as a legal association the network is complementary to these existing platforms.

2A22

Quantitative personalized oncology
- Mathematical models for precision radiotherapy

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Tumor growth and treatment response are remarkably complex, non-linear biological phenomena. Despite decades of research including clinical, population and basic science approaches, we continue to be challenged by the complexity, heterogeneity and adaptability of tumors in individual patients and across patient populations. Qualitative reductionism in artificial in vitro and in vivo modeling systems have lead to incremental increases in understanding tumor biology, often with limited success in translation to the human patient population in clinical studies. Prospective clinical trials predominantly focus on average outcome, with limited understanding why individual patients do or do not respond.

The uniqueness of each patient at presentation due to tumor and normal tissue intrinsic properties creates a highly patient-specific set of circumstances, which can impact greatly on clinical response. The future of radiation oncology practice needs to focus on selecting the most applicable dose and dose fractionation to provide tumor control whilst sparing organs at risk for individual patients prior to clinical intervention, and on continuously evaluating response and dynamically adapting to alternative protocols if necessary. Personalized medicine promises to deliver the right treatments in the right combination at the sequence at the right time to the right patient. We foresee a vital role for integrated mathematical modeling in achieving precision radiation oncology. Using retrospective data to forecast the behavior of complex dynamic systems using dynamic mathematical models has a long history. With ample radiation oncology experience, a wealth of historic patient response data, and quantitative methods already established, the personalization of radiation oncology may lead the way into the era of precision medicine.

2A23

Medical Radiation Protection Research Strategies in Europe And the role of the Medical Physicist in Europe

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Over the last decades, there has been a strong movement within Europe to build up strategic research agendas and set up platforms of interested people to foster this approach for the strategic planning of research in Europe. This has been applied to radiation protection research especially successful with the set-up of MELODI (Multidisciplinary European Low Dose Initiative), EURADOS (The European Radiation Dosimetry Group), ALLIANCE (European Radioecology Alliance) and NERIS (European Platform on preparedness for nuclear and radiological emergency response and recovery) and their corresponding SRAs. For many years, a medical approach was missing in terms of research regarding radiation protection for medical applications of ionizing radiation. Therefore, MELODI and EURADOS set up a memorandum of understanding with the medical associations using ionizing radiation in Europe: European Association of Nuclear Medicine (EANM), European Federation of Organisations for Medical Physics (EFOMP), European Federation of Radiographer Societies (EFRS), European Society for Radiotherapy and Oncology (ESTRO) and European Society of Radiology (ESR). In addition within the OPERRA project a task was funded to revive the medical radiation protection field. This task together with the memorandum of understanding was used by the five associations mentioned above to set up a first strategic research agenda. In the talk this strategic research agenda, which can be found on the internet or as a peer-reviewed paper in Insights into imaging in 2017, will be presented and explained. The structure is built along the lines of the main aspects of radiation protection in medical application of ionizing radiation. It puts a strong emphasis on the necessity of a clear transfer strategy of the research results into clinical practice and to harmonise practice throughout Europe. This will be explained in the talk as well as some major aspects of the content of the strategic research agenda.

During the exercise of building such a strategic research agenda it became very clear that it is necessary to

a) Keep this document a living document and refresh it regularly
b) Further actions are needed to explain, promote and lobby for the content of the document
c) Build up structures to identify and foster groups for answering call or identified research needs.

Therefore, the five medical associations (EANM; EFOMP; EFRS; ESTRO; ESR) decided to set-up a platform for medical radiation protection research. This platform is called EURAMED (The European Alliance for Medical Radiation Protection Research) and it was raised as a Joint Initiative from EIBIR. In October 2017 it became a legal entity and we are now open for membership applications. Due to the process of setting-up a dedicated strategic research agenda for medical radiation protection it became more evident that this task is of great importance and that there are strongly related aspects with low-dose radiation research. Therefore in 2017 it was already possible to start with a large European commission funded project called MEDIRAD, which is combining medical radiation protection aspects with radiation biology, radiation epidemiology and other aspects of (low-dose) radiation protection research. This is a very convincing example on how it was possible with this EURAMED effort together with the other platforms to foster medical radiation protection research in

Europe. In addition, EURAMED was invited by the other platforms to take part in their common activities for example within the CONCERT EJP project.
Within the above mentioned strategic research agenda for many aspects reference is made to the European directive 2013/59, which is called pretty often, basic safety standard. This document decided upon within the European commission and parliament in 2013 is replacing three former separate directives which had been dealing with ionizing radiation and the protection against it. Within this basic safety standard there is a number of new functions / persons defined in radiation protection and especially also in medical radiation protection. One of these functions is the medical physics experts (MPE). In the talk the requested tasks as well as the requirements to the education for such a medical physics expert will be explained. There will also be a number of examples how this is or will be handled in the different member states. The historical context about the objectives of medical physicists in the past will be given and how this will be extended for what reasons. The directive 2013/59 has to be put in place by legal actions of each country in 2018.

The very interesting aspects is that this legal requirement fit very well with the requirements for meaningful research in the field of medical radiation protection as defined by the strategic research agenda or other documents provided in the meantime like strategic research statements, common roadmap between the platforms etc. It will also hopefully foster the development of the strategic research agenda further to implement new aspects like for example artificial intelligence or others into the tasks. It can be foreseen, that a very solid ground has been laid for novel and meaningful research in medical radiation protection and its implementation into clinical practice for the benefit of the patient using expertise of all participating professions including medical doctors and to a large extend medical physicists. It is our obligation to make the best out of this chance and we would be happy to share our experience with all those interested outside Europe.

3M01

BER2018 Presentation Abstract

Dr Jacques Repussard (France), MELODI Past president

Title: Understanding low dose radiation exposure effects : MELODI's views on developing international cooperation

Abstract:

In the aftermath of the Chornobyl nuclear accident which affected directly most European countries to various degrees, and also in the context of fast growing medical use of radiation for imaging and therapy purposes, the health risks associated to low dose radiation exposure have become an issue of societal concern. Unfortunately this concern is compounded by the fact that science is so far unable to provide satisfactory answers about health risks related to such exposure, due to significant remaining uncertainties, both in the understanding of underlying biological phenomena associated to such exposure, and in the data resulting from epidemiological studies.

In this context MELODI was set up a decade ago, in order to facilitate the steering of research strategies and thus focus efforts on priorities aiming at reducing such uncertainties. This needed a special cooperation between research policy makers at European and national levels on one hand, and the competent communities in the scientific disciplines concerned by low dose effects research on the other hand, which was illustrated by the publication by the European Commission, in 2009, of the "Report on European low dose risk research" of the "High Level and Expert Group" (HLEG).

MELODI's key operations lead to the development and annual updating of a Strategic Research Agenda (SRA) and derived initiatives concerning education and training and scientific research infrastructures. These documents serve as a basis for the definition of research and training calls which are published periodically by EURATOM, or broad ranging EURATOM funded projects such as OPERRA, or more recently CONCERT, a project also co-funded by several EU member states.

The maturation of such strategies is slow, and a first positive result has been the widespread understanding that the answers to the questions raised in the MELODI SRA could not be discovered without intense and long range focused multidisciplinary cooperation, bringing together biology, medicine and molecular epidemiology, a mode of work which is gradually recognized as the best way forward.

Of course, there is no reason why such a scientific cooperation model should be restricted to the European research community. Indeed, considering the complexity of the biological phenomena to be investigated in order to fully explain the many effects (harmful or not) of human low dose ionizing radiation exposure, there is a strong argument to promote the development of such multidisciplinary approach in a multilateral context associating countries which have so far provided major scientific results contributing to the understanding of low dose radiation effects, such as Japan and the USA. However, an effective move in that direction will require the development of an appropriate multilateral framework going beyond the traditional bilateral arrangements, with the active support of research policy makers at governmental level, and of the leadership of the scientific communities in the disciplines concerned. Such an initiative would most certainly be welcome by international organizations such as NEA, IAEA, WHO and ICRP.

3M02

Electric Power Research Institute International Dose Effect Alliance

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The Electric Power Research Institute (EPRI) is a non-profit research organization dedicated to the public benefit and the advancement in electrical power. EPRI is structured with a number of sectors, with nuclear generation being one such sector. EPRI interest in low dose and dose rate ionizing radiation effects dates back almost 10 years, with the initiation of activities to support the need to better understand the relationships between radiation dose, and health impact implications. In 2015, EPRI identified the need for a forum to exchange information on research programs and results on a global scale and initiated the International Dose Effect Alliance (IDEA). The vision of IDEA is for an international platform for information exchange, discussion, cooperation, and collaboration in low dose radiation research. The first workshop was held in November 2016, and a second workshop was held in December 2017. Amongst other outcomes from the December 2017 workshop, a facilitated discussion of participants identified priorities for research, including: communications; individual sensitivity and susceptibility; data capture and model creation; integration of epidemiology and biology; mechanisms of cancer and biomarkers; and non-cancer effects. Looking forward, EPRI plans to continue cooperation with international organizations and groups on alignment of strategic research agendas, and collaborations to begin development of models that can bridge the gap between radiation biology studies and results of epidemiological cohorts.

Abstract for the International Workshop on the Biological Effects of Radiation
- Bridging the gap between radiobiology and medical use of ionizing radiation –

3M03

Low-Dose Radiobiology Program at Canadian Nuclear Laboratories: Past, Present and Future

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Canadian Nuclear Laboratories, Chalk River, Ontario, Canada

In recent years, it has been increasingly acknowledged that achieving climate change goals set forth at the Paris Conference of Parties to the United Nations Framework Convention on Climate Change may not be possible without nuclear power generation. However, world-wide acceptance of nuclear power as a major contributor to climate change control is dependent on a robust and reliable system of radioprotection. Such system needs to be scientifically justified. Yet, the current international system of radioprotection that is based on the Linear-No-Threshold (LNT) hypothesis falls short of such requirement. Large body of scientific evidence shows that biological responses of cells and organisms to low doses of ionizing radiation (LDR) are not linear. As a result, continuous and heated debates about the ability of the LNT model to predict human health risks associated with exposure to LDR occur among various communities, including the scientific community. To rectify this controversy, there is a need for large-scale international collaborative groups and consortia aimed at carrying out relevant biological studies using a combination of experimental approaches. The single most important feature of such studies appears to be the broad coverage of biological responses to LDR exposure – from early DNA damage and DNA damage signalling events to long-term health outcomes, such as cancer, all studied and considered within a single context. The resulting deep scientific understanding of the effects of LDR can be used to improve the radioprotection system.

To address this need, a comprehensive low-dose Radiobiology research program has been established at Canadian Nuclear Laboratories (CNL), formerly known as Atomic Energy of Canada Limited. CNL is a federally and privately funded Science and Technology organization that undertakes research and development (R&D) activities in various areas of Nuclear Sciences, including Radiobiology. CNL has a strong and reach legacy in Radiobiology, in particular low-dose Radiobiology. The Biological Research Facility build at CRL in 1990s is equipped with a low-dose animal irradiation hall called the Gamma Beam. It is located within the boundaries of a specific pathogen free animal facility such that chronic low-dose irradiation experiments can be performed continuously during the entire animal life span. This globally unique facility has been home to various large scale low-dose mouse in vivo studies that made substantial contribution to the filed. Thus, studies lead by Dr. Mitchel at CNL and showing that LDR delays the onset of endogenous tumorigenesis in mice in vivo (*1, 2*) has been cited more than 100 times each, providing a foundation for subsequent mechanistic mouse studies. These reports were preceded by earlier highly cited in vitro studies demonstrating radioadaptive responses in mammalian cells (*3, 4*). In late 2000s, low-dose Radiobiology program at CNL was expanded and enhanced to include molecular biology, immunology, epigenetics and other approaches, which allowed studying biological effects of LDR at broader and deeper levels. This was accompanied by partnering up and leveraging the CNL program with international organizations and consortia, such as European Union (EU) funded NOTE program (Non-Targeted Effects) and the French Institute of Radiological Protection and Safety (IRSN). Beside the mandate from the Government of Canada, various other national and international stake holders, such as Health Canada, Canadian Nuclear Safety Commission and CANDU Owners Group, expressed strong support in the low-dose Radiobiology program at CNL. As a result, world-wide

recognition of the CNL Radiobiology program continues to grow evident from recent scientific publications and the involvement of CNL scientists at international forums and programs as invited speakers and/or experts in low-dose Radiobiology.

Recent studies carried out at CNL showed that spleen lymphocytes from mice exposed to low-dose gamma-radiation exhibited higher DNA repair capacity via nucleotide and base excision repair pathways. Interestingly, DNA double-strand break repair was not affected. Consistent with this, LDR-exposed cells in vitro had a delayed onset of senescence or cellular aging. This was accompanied by a substantial changes in miRNA expression profiles, suggesting a strong role of epigenetic mechanisms in LDR effects. These results were partially confirmed in the in vivo mouse model of aging using markers or aging assessed in the kidneys of aged control or aged LDR-exposed mice. Additionally, we demonstrated that LDR exhibited overall stimulatory effect on the immune system of mice in vivo. Cancer, being an aging related disease, has a strong mechanistic overlap with aging (*5*), with the immune system playing crucial role in tumorigenesis (*6*). Our results therefore provide a link between early DNA damage and repair responses and late systemic outcomes, such as modulation of the immune system and aging, all converging on and affecting tumorigenesis. Furthermore, our most recent results showed that LDR exposure of muscle stem cells partially restored their aging-related decline in function (muscle fibre formation). Our current studies are aimed at obtaining even deeper insight into mechanisms underlying responses to LDR and affecting systemic health risks - through all levels of biological organization, from molecules to tissues.

With closure of the low-dose radiation research program funded by the U.S. Department of Energy in late 2000s, the CNL low-dose Radiobiology program remains one of the world largest efforts in the field. Unlike former and current EU low-dose research programs (DoReMi, MELODI, CONCERT) that provide support to dozens of independent laboratories and whose research priorities may not necessarily lie within low-dose Radiobiology, the CNL based program is specifically dedicated to and focused on this area. Being centrally coordinated and overseen, supported by unique facilities and a skilled professionals, the CNL low-dose Radiobiology may be viewed as a centre of excellence in low-dose radiation research. Nonetheless, our team strives to build further links with laboratories, organizations and programs world-wide that are strongly dedicated to understanding the biology of LDR effects.

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3M04

Planning and Acting Network for Low Dose Radiation Research (PLANET) and promotion for integrated network in Japan

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There are important issues for low dose exposure, especially decreasing uncertainty of risk estimation of low dose/low dose-rate exposures. Desirable approach is to establish mechanistic and numerical model based on stem cell biology and radiation biology at high dose rate, and then to underpin the selection of appropriate risk model of chronic exposures.

In order to carry out these researches steadily and continuously, it is necessary to promote collaboration among stakeholders in and outside Japan. Therefore, we decided to establish all-Japan network among regulators, academia and research institutes, and other stakeholders (incl. industries). The tentative name of the network is PLANET; Planning and Acting Network for Low Dose Radiation Research.

National Institute of Radiological Sciences (NIRS) set up preparatory committee for PLANET in 2016 and appointed 9 specialists for radiation protection, radiation biology, epidemiology, and dose assessment, and summarized the results on the report (1). The preparatory committee discussed issues for research to improve risk estimation and identified 5 priorities the issues and needs, as follows; 1) Epidemiological studies of the low dose/low dose rate radiation designed for a risk evaluation appropriately, 2) Studies of the mechanism elucidation for risk evaluations of the low dose/low dose rate radiation, 3) Integrate studies to use animal experiment data for the interpretation in the epidemiological studies, 4) Studies to elucidate the association between age, sex, heredity factor, lifestyle and radiation, 5) Database compilation including negative data and saving archives of experiment samples.

The preparatory committee also discussed a collaborative system of PLANET involving all sectors in Japan, including authorities, academia, universities and research institutes of radiation research, and proposed support system for cooperation and collaboration researches among related researchers and institutes. This cross-sectoral network should also aim to work together with international organizations and cooperation both in Japan and abroad.

Nuclear Regulation Authority (NRA) entrusted NIRS with a strategic promotion for the radiation safety and protection research from 2017. This promotion is intended to supports the setup of the networks for problem solution to radiation protection and build an umbrella type platform which integrates the networks. In addition, the promotion extracts the priority theme of the radiation safety and protection research.

During the first year of this promotion, NIRS asks Japan Health Physics Society, Japanese Society of Radiation Safety Management, the Japanese Radiation Research Society, Japanese Association for Radiation Accident/Disaster Medicine and PLANET for the suggestion of the priority theme of the future radiation safety and protection research. The theme of the research is divided into 6 general categories; 1) Biological effect and risk, including low dose/low dose rate radiation effect, 2) Safety use of the radiation, 3) Measures taken against nuclear and radiation accident, 4) Environmental radiation and radioactive waste, 5) radiation measurement and estimation, 6) Radiation education and risk communication.

A meeting to report the results is held to perform an argument for the consensus building in the umbrella type platform about the priority theme of the research. Finally, NIRS submits the report about the priority theme to NRA, and NRA decides the theme of the next promotion in reference to the report.

PLANET is a network for low dose/low dose rate radiation research including basic science. Multidisciplinary experts of PLANET contribute to a basic and regulatory science about low dose/low dose rate radiation risk evaluation.

Acknowledgements: Thanks to Dr. Kazuo Yoshida and Dr. Toshiyasu Iwasaki, Central Research Institute of Electric Power Industry, who contributed PLANET

(1) Report of the preparatory committee for PLANET (Japanese);
http://www.nirs.qst.go.jp/publication/radiation_risk/01.pdf

3M05

JSPS committee “multidisciplinary research on the biological effects of radiation”

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In order to promote the research in low dose and low dose-rate radiation, as well as in medical radiation, we established a committee “Multi-disciplinary research on the biological effects of radiation” in JSPS (Japan Society of Promotion of Science). The aim of the committee is to promote the inter-disciplinary discussions on the biological effects of radiation and to enhance multidisciplinary researches in these fields so as to integrate individual knowledges in various fields.

After the accident at Fukushima Daiichi Nuclear Power Plant in March 2011, it became immediately clear that the accurate, science-based information regarding risks of radiation exposure was scarce. A serious divergence in views has emerged between physics and biology, medical providers and researchers. Researchers in various fields such as epidemiology, animal experiments, cell research, and molecular biology have been making much progress with their studies on health effects of ionizing radiation. More than a century of radiation research has provided us with extensive information on health effects and biological mechanism caused by radiation exposure, especially for moderate to high dose radiation. This has contributed especially in determining the standard criteria of radiation protection. However, there has not been a consensus on the biological effects of low dose radiation and, in particular, low dose-rate radiation mainly due to the lack of inter-disciplinary communication. Multidisciplinary collaboration is truly needed to solve the long-standing problems in biological effects of radiation.

As one of the main topics of this committee, we promote inter-disciplinary discussions between radiobiologists and medical researchers. Rapid increase in radiological procedures during the past century has made significant contribution to the human health. Nowadays, medical radiation has become a major source of human exposure to ionizing radiation. Such widespread use of ionizing radiation in medical practice alerts the medical community to carefully optimize the procedures considering the benefit and risk of each patient. However, the health effects have not been confirmed for low dose and low dose-rate of radiation exposure. As medical use of radiation is expected to expand globally, the scientific research to clarify the biological effects of low-dose and low-dose-rate exposure is essential not only for optimization of the current procedures but also for future development of new technology. We believe the integrative efforts of multidisciplinary fields will solve the problem. We hope that this international workshop will ignite such activities.

3A11

Radiation protection in therapy with radiopharmaceuticals

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Introduction

Radiation protection in medicine covers in principle, medical exposure, occupational exposure, and public exposure in association with various clinical circumstances. Medical exposure involves not only patients but also their comforters and carers, and volunteers in biomedical research. Medical exposure of patients has unique features that affect how the fundamental principles are applied [1]. Application of dose limits, which is one of the fundamental principles of radiation protection elsewhere, is not undertaken in medical exposure. This is because such dose limits would often do more harm than good in the course of treating patients. Two fundamental principles of general radiation protection, justification and optimization, apply in medicine in a different way. Justification in radiation protection of patients is unique in that the very same subject enjoys the benefits and suffers the risks associated with a radiological procedure. Optimization of protection for patients is also unique in that radiation therapy gives intentional radiation for the purpose of treatment, and diagnostic procedures give the benefit and the risk to the same subjects. Therapy with radiopharmaceuticals, namely radionuclide therapy (RNT), requires deliberate radiation protection standards because it uses unsealed radionuclides and gives therapeutic radiation doses in humans.

From Radionuclide Therapy to Theranostics

The use of radiopharmaceuticals for therapy using novel radionuclides, including alpha emitters, compounds and probes, has been increasing for the treatment of various tumors, that is, RNT, in connection with which “theranostics” has been established. Theranostics means a method of combining diagnosis and therapy and enhancing the efficacy and safety of procedures to an individual patient. In nuclear medicine, theranostics usually refers to a combination of imaging and RNT in oncological nuclear medicine [2]. Conventional imaging and treatment of iodine-131 therapy for differentiated thyroid cancer, and Zevalin therapy with indium-111 antibody and yttrium-90 antibody to B-cell non-Hodgkin's lymphoma can be examples of theranostics.

Dosimetry-guided Personalized Therapy

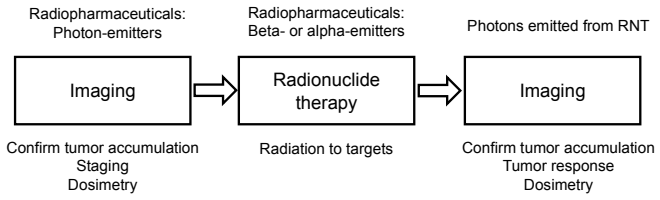
As theranostic procedures currently attracting attention in nuclear medicine, somatostatin receptor imaging for neuroendocrine tumors and PRRT (peptide receptor radionuclide therapy) have attracted attention, and a large-scale clinical trial of Lutetium-177 Dotatate against neuroendocrine tumors has been conducted [3]. Also, imaging with Ga-68 labeled ligands targeted to PSMA (prostate specific membrane antigen) expressed in prostate cancer and RNT with Lu-177 labeled ligand are currently being conducted mainly in Europe. In addition, alpha-emitter Ac (actinium)

-225-labeled PSMA ligand has been reported to have a dramatic therapeutic effect on advanced prostate cancer [4]. In these procedures, dosimetry based on imaging is critical in guiding subsequent therapies. The European directive on basic safety standards (Council directive 2013/59 Euratom) mandates dosimetry-based treatment planning for radiation therapies including radiopharmaceutical therapies. The directive comes into operation February 2018. Dosimetry-guided practices will have significant implications for the evolution of RNT (Figure 1).

Conclusions

RNT combined with imaging and dosimetry is undergoing a significant expansion, and such dosimetry-based treatment planning is already in place. The mandated individualization is likely to improve the effectiveness of the treatments [5].

Figure 1. Radionuclide Therapy guided by Imaging and Dosimetry



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3A12

Experimental evaluation of the carcinogenic effect of carbon ions and neutrons in children

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Ion beam radiotherapy is a form of cancer therapy which uses accelerated ions such as carbon ions and protons. As compared with protons, the use of carbon ions is considered to improve treatment by permitting more accurate dose localization and stronger cell killing attributed to the sharp Bragg peak and high linear energy transfer (LET). NIRS has been one of the leading institutions of carbon ion radiotherapy in the world.

Radiation types relevant to ion beam radiotherapy

Because Bragg peaks of ion beams are normally too narrow for therapeutic applications, spread-out Bragg peaks (SOBP) have been devised to obtain a broad and uniform dose distribution. In carbon ion radiotherapy, fractionated irradiation with a beam with 6-cm SOBP, which is developed from the 290-MeV/u carbon ions and has an LET range of 40–90 keV/μm within the SOBP component, has been used to treat several cancer types. Normal tissues can be exposed to 1) the plateau region of the carbon ion beam, which has a lower LET of 14 keV/μm, and 2) fast neutrons, which are generated at the collimators and in the patient body, having a broad energy spectrum covering the most biologically potent band of 0.1–2 MeV. Dose evaluation studies have indicated lower neutron dose in carbon ion radiotherapy than proton radiotherapy.

Second cancer risk from ion beam radiotherapy

Although such advances in therapy have contributed to longer survival times of patients, late sequelae of therapeutic treatments are in turn becoming the next concern. Among the most serious of such sequelae are second cancer, for which conventional forms of radiotherapy are an established risk factor. Young cancer patients are especially affected by this issue, as they are expected to live a longer life than older patients. Advance in ion beam radiotherapy led ICRP to publish a recommendation on relevant radiological protection (Yonekura et al. 2014), although the issue of second cancer was not much discussed because of the scarcity of evidence. Major scarcity lies in the information on the carcinogenic effect of relevant radiation species, as compared to low LET radiation (such as γ rays), required in predicting second cancer risk.

Animal experiments to measure risk of carcinogenesis

Breast cancer is a common second cancer accompanying conventional radiotherapies of childhood and adult cancers. We used the rat mammary carcinogenesis model to study the effects of γ rays (^{137}Cs), carbon ions (290 MeV, 14 keV/μm) and fast neutrons (2 MeV) irradiated at different ages on subsequent development of breast cancer (Imaoka et al. 2013, 2017). Female rats at 1, 3 and 7 weeks of age (neonatal, prepubertal and postpubertal, respectively) were whole-body irradiated with γ rays (0.2–2.0 Gy), carbon ions (0.2–2.0 Gy) or fast neutrons (0.05–1.0 Gy) and were observed for development of mammary carcinoma until 90 weeks of age. The highest dose of all radiation types resulted in premature cessation of estrous cycling (a phenomenon analogous to menopause in women) and low cancer incidence in the 1-week groups. Otherwise, the effect of γ rays per unit dose was essentially similar among the age groups. The effect of carbon ions and fast neutrons, in contrast, was most prominent when rats were irradiated at 7 weeks. Thus, the three types of radiation impose breast cancer risk that exhibits distinct age dependence in rats. Relative biological effectiveness (RBE) is a measure for the biological effect of a certain type of radiation as compared with a reference, low LET radiation. Mathematical analysis of the above data indicated that RBE values of carbon ions and fast neutrons should be separately estimated in animals of different ages. The estimated values may be taken into consideration in predicting second cancer risk in clinically relevant situations.

Conclusion

Estimation of the RBE value of accelerated carbon ions and fast neutrons for carcinogenesis is an important issue in predicting the risk of second cancer after carbon ion radiotherapy. Animal experiments like ours can offer important information in this regard.

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3A13

Second cancer after radiotherapy

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A word of History

Radio-induced cancers were detected very early in the history of Radiology and Radiotherapy: a first case was reported as soon as 1902 by Frieben, and subsequently, a number of pioneers paid a heavy tribute to their work with radiation : among them, Marie Curie and Irène Joliot-Curie, whose deaths (by Myeloblastic Aplasia and Chronic Myeloid Leukemia, respectively) were clearly related to a whole life devoted to their study of Radiations.

The dramatic consequences of the Hiroshima and Nagasaki bombing, in August 1945, unfortunately achieved to prove, if necessary, the carcinogenic risks of high doses of Ionizing Radiations. In spite of such evidence, we have to recognize that, for decades, radiation oncologists did not consider the carcinogenic risk of their therapeutic irradiations as being a real topic of concern.

The relative lack of interest, for years, of radiation oncologists for the carcinogenic risk of the therapy they applied, is most probably due to the poor survival results of radiotherapy in the first half of the XXth century. Moreover, at that time, a patient surviving more than 5 years was usually considered as being cured, and his follow-up was stopped (although we now know that most radio-induced cancers are emerging more than 5, and even 10 - 15 years after irradiation).

It was only in the sixties-seventies that some pioneers clinically detected an excess of second cancers after radiotherapy. In the eighties, the prominent role of the irradiated volume was demonstrated, as well as the higher risk of radio-induced cancers in young adults, and even more in children. Today, in 2018, the carcinogenic risk of any radiotherapy has been extensively studied, and this risk must be kept in mind when deciding the therapy and when treating the patients.

Second cancers; radio-induced or not ?

The wording “second cancer” needs to be clarified. Cancer unfortunately remains a frequent pathology, and it is clear that to have been the victim of a cancer does not “protect” against a second one. Moreover, the cause of the first cancer (genetic predisposition, or way of life -see above-) may remain, and may favor the emergence of a second one.

It is therefore difficult to identify the “second cancer” cases which can be considered as radio-induced, and those which are clearly not related to irradiation. Up to now, we do not have available, except in rare specific cases, any specific genetic mutations which would prove the radiogenic cause of a “second cancer”.

The study of large cohorts shed some light on this problem: In the extensive 2007 review by Suit, the relative risk (RR) for a second primary cancer in 11 cohorts of cancer patients was as high as 1.31, when comparing the radiotherapy patients (RT) and the general population (GP): RR RT/GP = 1.31 (95% CI; 1.15 - 1.49). It therefore appears that cancer survivors do have a higher risk of developing a “second cancer”.

However, the real risk of radio-induced second cancers is better evaluated by the RR : “RT/nonRT”, which compares the cancer patients who received an irradiation to those that did not receive any irradiation. This relative risk RT/nonRT in the Suit’s study is 1.08 (95% CI: 1.00-1.17). This last RR “RT/nonRT” gives a better indication of the carcinogenic role (borderline significant) of radiotherapy.

Berrington de Gonzalez , in 2011, concluded , after a large cohort study, that a relatively small proportion of second cancers (about 8% of all « second cancers ») are related to radiotherapy in adults, suggesting that most are due to other factors, such as lifestyle or genetics.

Radio-induced cancers: lessons from the literature

A huge number of reviews are now available in the literature, including the one performed by an ICRP/ICRU task group (unfortunately unpublished to date) and a recent 2017 AAPM document (AAPM TG 158). From this large experience, can be extracted a few main points:

1/ Cancer patients are at a higher risk for developing secondary cancers than the general population, but - see above - radiotherapy is only responsible for a (small) proportion of the second malignancies.

2/ The clinical data emphasize the *role of age*, with children being much more sensitive to the carcinogenic effect of ionizing radiations than adults (a 3-6 fold increase).

3/ The reviews of available data confirms the clinical experience, according to which " the majority of second induced cancers occur in or close to the high-dose treatment volume" (Hall 2006).

4/ The relative risk appears to be different for different organs, with the thyroid probably being the best example of an organ particularly sensitive to the carcinogenic effect of radiation, especially in children.

5/ The relative risks of radio-induced cancers tend to be lower in the medical cohort studies than in the Japanese A-Bomb survivor studies (Little, 2001). The fractionation /protraction of most of the therapeutic irradiations, as well as the neutron component in the A-bomb data may account for this difference (Schneider 2008).

Radiobiological models

The dose/effect model (or risk model) to be used for radio-induction of cancers remains in 2018 a burning and endless topic.

A number of authors stick to the Linear-No-Threshold (LNT) model, whatever the dose, thus from zero Gy until the large doses of 70-80 Gy of radiotherapy.

The LNT model was mainly derived from the data observed after Hiroshima and Nagasaki, data which showed a clear linear relationship between 0.5 and a few grays. This is often considered as the "Gold standard", but

- Even in the dose range mentioned above, we previously saw that this model, based on atomic bomb survivors, could overestimate the risk in the medical radiotherapy series.
- For low doses (below 0.5 Gy), radiobiologists are still fighting, some of them sticking to the LNT model, some others proposing a threshold (or at least a "practical" threshold, generally about 100 mSv), and finally others describing an *underestimation* of the risk by the LNT model…
- For "high doses" (above a few grays, but with large variations from a study to another); three models are in competition; the LNT one (which would suggest a very high -unrealistic?- risk at radiotherapy doses), the "bell-shaped" model, following data, some as old as 1957 by Gray himself, showing a *decrease* of the risk at high doses, and several "plateau" models, where the risk is "plateauing" after a certain dose.

While the battle is not finished, we can only very prudently suggest that the presently available clinical data seem to better support some "plateauing" at very high doses.

Which recommendations in 2018 ?

The ICRP/ICRU task group and the AAPM TG 158 document proposed recommendations (actually almost identical) to try and reduce the risk of secondary radio-induced cancers after radiotherapy.

While radiation oncologists and physicists are today well aware of the advantage of reducing the volumes irradiated at high doses, with more and more sophisticated techniques (IMRT, VMAT, Gating and tracking, IGRT …), in parallel, it is imperative that those same professionals understand the magnitude of the dose levels *outside of the treated volume*, and are aware of methods to manage them.

The low doses outside the target volumes have been neglected for too long, and the profession is facing a new challenge; to reduce as much as possible the deterministic effects, and the carcinogenic risk close to the target volumes, while reducing at the same time the "low doses" far away from the treated volume, in order to avoid radio-induced cancers in those areas.

Actually, such a caveat had been well emphasized in ICRP publication 73, subsequently followed by the European Directive 97/43 : *« For radiotherapeutic purposes, exposures of target volumes shall be individually planned; taking into account that doses of non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure. »*

We summarize here the main recommendations for reducing the risk of radio-induced cancer after radiotherapy:

1. Adapting the irradiation technique
   - AAPM TG 158 emphasized the trade-off of modern IMRT (Intensity Modulated Radiotherapy) treatments, relative to 3D CRT. IMRT allows decreased treated volume through increased conformality, which will reduce the volume of tissue receiving a high dose. However, this is done at the cost of increased head leakage from increased number of Monitor Units (MUs), which increases doses farther from the target, and thus the "integral dose" (the total energy absorbed by the body).
   - The more recent VMAT (Volumetric Modulated Arc Therapy) technique is using less MUs, and therefore allows to reduce the "integral dose".
   - Flattening filter; for both IMRT and stereotactic procedures, the out-of-field dose is reduced when the flattening filter is removed from the beam line, so FFF (Flattening Filter Free) delivery is an improvement in terms of reduction of the integral dose.
   - Photon energy: here again the radiation oncologist has to face a trade-off between high- and low-energy treatments. High-energy therapy is associated with some (fortunately low) neutron production. Low-energy therapy results in higher stray photon dose because of the greater number of MUs required. Although difficult to precisely quantify, the added neutron contamination at high energy seem to be offset by the added stray photon dose at low energy. For the AAPM TG 158, the optimal energy could be an intermediate such as 10 MV.
   - Proton therapy allows a substantial reduction in dose distal to the target, resulting in reduced integral dose (typically by a factor of 2 - 3 compared with IMRT).

2. Reducing the target volumes
   - The larger the irradiated volume, the higher the risk of a secondary radio-induced cancer. Reducing the size of the CTV or PTV can be one of the most potent options for reducing the dose to nontarget structures (AAPM TG 158).
   - In clinical practice, the CTV has already been reduced in many clinical situations. For Hodgkin's lymphoma, for example, the former large field irradiation has been replaced in most cases by the treatment of the involved regions only, with already a positive impact on the risk of radio-induced cancers. In some other cases, the irradiation of some "prophylactic" lymph node areas could be omitted (For testicular, breast and prostate cancers, for example).
   - Reducing the PTV margin can be a simple way to decrease the irradiated volume, but one should keep in mind that such a margin reduction is typically associated with increased imaging (see below).

3. Adapting to patient's age
   - As previously shown, children are much more prone than adults to develop a radio-induced second cancer after a given dose of irradiation. There is no "cut-off" for risk depending on age; the risk, being very high for the newborn, decreases progressively with age.
   - In children, when irradiation cannot be omitted, everything should be done to reduce both the target volume extent and reduce the integral dose.
   - In such a setting, proton therapy has been more and more proposed.

4. Adapting to specific organs
   - All organs do not demonstrate an equal risk of a secondary radio-induced cancer. Some of them, such as the small intestine, are less sensitive to cancer radio-induction, while thyroid and breast are examples of organs highly sensitive to radiocarcinogenesis, a feature highly amplified by the age factor (with a high susceptibility in children).

5. Imaging dose management
   - IGRT (Image Guided Radiotherapy) has become compulsory when using new highly precise treatment technologies. However, it brings an additional dose that should not be ignored.
   - Radiation oncologists should be aware of the dose delivered by the IGRT they are using, and should adapt the number of controls to each patient's case.

6. Other procedures to reduce the risk of radio-induced cancers

- They are based on procedures aiming at reducing as much as possible the “Integral dose”, and have been presented in detail in the AAPM TG 158 document;
- Avoidance of physical (or mechanical) wedges, responsible for an out-of-field dose higher by a factor of 2 - 4 relative to an open field, use of tertiary Multi Leaf Collimators (MLC), choice of the beam angles, jaws tracking, patient shielding, and accelerator shielding are other solutions to reduce the integral dose.

Conclusions

Even if radio-induced cancers are rare, they must be kept in mind each time radiotherapy is proposed.

It had been pointed out that new technologies, such as IMRT, were responsible for an increase in the (low) doses received out of the field. Fortunately, such a dose increase at distance is largely offset by the very significant reduction of the areas receiving high doses (areas where the risk of radiocarcinogenesis is much higher). Finally, even if new technologies were not considered to cause more second radio-induced cancers than conventional techniques, *a continual effort should be made to reduce the out of field doses delivered to patient(s)* as a continued radiotherapy improvement strategy, thus following previous ICRP recommendations concerning optimization.

Age is one of the key parameters impacting on the risk of radio-induced secondary malignancies. Children could be nearly 3 to 6 times more sensitive to the carcinogenic effect of radiation than adults. Consequently, all efforts should be made to reduce the risk in children. In contrast, the second cancer risk is much lower, or even nil, in the elderly. In between, the secondary cancer risk, although most often low, should be kept in mind when designing therapeutic schemes and/or prescribing a specific irradiation.

3A22

Low-dose CT screening for lung cancer

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Lung cancer is a leading cause of cancer death in Japan. Though smoking is the greatest risk factor for lung cancer death, Asian have a relatively high risk of lung cancer among nonsmoker compared to the Caucasian. In addition, nonsmoker's lung cancer is increasing in Western countries. Since the risk of lung cancer due to secondhand smoke has also been reported, death from lung cancer is a serious issue regardless of smoking history.

Lung cancer screening using low dose CT (CT screening) was initiated in Japan, United and in Europe around early 1990's. It was reported that many earlier, smaller lung cancers can be detected by CT screening compared with conventional chest X-ray. In 2011, National Lung Screening Trial (NLST) reported that annual CT screening for high risk participants leads to 20% reduction of lung cancer death[1]. Recently, European position statement on lung cancer screening recommended that European states demand to determine a timeline for implementing lung cancer screening[2]. There is a possibility that CT screening for high risk participants will be spread in western countries.

Though the effectiveness of CT screening for nonsmoker and light-smoker is still unclear, CT screening in Japan has been provided to people other than heavy smokers. The results of ongoing randomized controlled trial (JECS study) are expected[3]. In addition, it is desirable to evaluate the results of screening by observational studies.

In Hitachi City, Ibaraki Prefecture, CT screening for 50 years or older citizens initiated

in 1998, and 30% of the citizens received CT examination at least once by 2006. We reported excellent survival (5-year survival of 90%) of 210 cases of lung cancer detected by CT screening. Furthermore, based on time trend analysis, a significant reduction (24%) in lung cancer mortality was observed 4 to 8 years after introduction of CT screening among Hitachi residents[4]. This finding suggests that wide implementation of CT screening can decrease lung cancer mortality at community level. Currently, we are conducting a cohort study of CT screening participants and X-ray screening participants among Hitachi residents.

CT screening images can detect various smoking related findings represented by the pulmonary emphysematous change (CT emphysema). We reported that CT emphysema is an important radiological risk factor for future abnormality of respiratory function. If we can evaluate the risk of respiratory disease and comorbidity according to the images, the benefit of screening is expected to further increase.

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3A23

Development of Low Dose Diagnostic CT

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Since the first diagnostic CT scanner was produced in 1972, its performance has been continuously improved by series of innovations, such as helical scan technique, multi-slice detectors, ECG gating scan, sophisticated reconstruction algorithm, and so on. These innovations enabled many new scan techniques which could provide us with new or more accurate diagnostic information. On the other hand, some of them such as cardiac gating scan, dynamic hepatic scan, and perfusion scan require higher radiation dose. As the total number of CT scans increases, the associated risk of radiation became a social concern. Canon Medical Systems (formerly Toshiba Medical Systems) has been developing and manufacturing CT systems over 40 years. Throughout its history, we have been continuously introducing new technologies to reduce radiation dose so that new scan techniques could be clinically acceptable and thus expanded the clinical value of CT systems. Followings are examples of such technologies:

(1) higher output with lower noise from detectors to achieve better SNR in raw data.

(2) X-ray tube current modulation to dynamically control X-ray output depending on the body thickness, heartbeat, and breathing cycle.

(3) active collimation to shield X-ray at the scan start and end position in a helical scan which does not contribute to output images.

(4) dynamic scan condition control to adjust scan parameters during a helical scan depending on the patient body part

(5) iterative reconstruction algorithm to achieve higher resolution while reducing image noise by introducing various physics models into the reconstruction algorithm

We continue our research and development to enhance capability of a CT scanner while reducing the radiation dose and thus expand its clinical value.

Abstracts of Poster Presentations

P01	The influence of low dose-rate radiation on the mutation frequency in Drosophila : Tomonori Onishi (Kansai University)
P02	Two-step model for the occurrence of retinoblastoma : Tetsuhiro Kinugawa (Kansai University)
P03	Analysis of Childhood Thyroid Cancer Incidence in Fukushima based on Dose Response Relationship : Takahiro Wada (Kansai University)
P04	Agendas and Issues of Participatory Dialogues by Junior-High and High School Students from Fukushim Hama-doori and Capital Area - "Exciting Class 2017" by Junior- and High Students on Thyroid Screening Test - Issues and Results of IWAKI Dialogues – : Tetsuo Sawada (Tokyo Tech.)
P05	The development of ESR dosimetry using human hair : Seiko Hirota (Hiroshima Univ. RIRBM)
P06	Particle Therapy System Simulation Framework and its application for probing material composition in patient body : Tsukasa Aso (National Institute of Technology, Toyama College)
P07	Twitter analysis of public response to radiation exposure after the Fukushima Daiichi Nuclear accident : Kazuko Uno (Louis Pasteur Center for Medical Research)

P01

The influence of low dose-rate radiation on the mutation frequency in *Drosophila*

Tomonori Onishi[1], Takahiro Wada[1], Yuichiro Manabe[2] and Masako Bando[3]
[1]Kansai University, [2]Osaka University, [3]RCNP, Osaka University

In 1927, Muller[1)] first reported that the artificial mutation frequency in *Drosophila* increased linearly with the total dose of X-ray irradiation. Later, it was found that the slope of this linear increase did not depend on the dose rate of the X-ray. In contrast to these results in *Drosophila*, Russel[2)] found in his Mega-mouse project that the mutation frequency in mice depends on the dose rate as well as on the total dose.

Now, we know that there are repair mechanisms against the damages to DNAs. In order to analyze the experimental data on the mutation frequency with chronical exposures, we need a theoretical framework which takes account of the repair (recover) mechanisms. We analyze the experimental data of the mutation frequency in *Drosophila* which was done by Purdom and McSheehy[3)] using a mathematical model, Whack-A-Mole (WAM) model, which takes account of the recover effects.

In WAM model, the mutation frequency is described with the following differential equation.

$$\frac{dF}{dt} = a0 + a1d - (b0 + b1d)F$$

Here, F is the mutation frequency, the term $a0+a1d$ is the rate of change from normal cells to mutated cells, and the term $b0+b1d$ denotes the decrease rate of mutated cells.

Purdom and McSheehy irradiated male *Drosophila* with both acute and chronical exposures with the same total dose (800rad). In the case of low dose-rate exposure (0.05 rad/min), the irradiation extended over the development period from larvae to adult. In the case of high dose-rate experiments (0.5 rad/min and 5.0 rad/min), in order to compensate the effects of the development during the chronical exposure, they divided the samples into several groups then each group was irradiated sequentially through the development period. Even with the same given dose with the same dose rate, the mutation frequency becomes smaller as the interval becomes longer. Even with the same given dose with the same dose rate, the mutation frequency becomes smaller as the interval becomes longer. By taking account of the interval between the exposure and the mating.

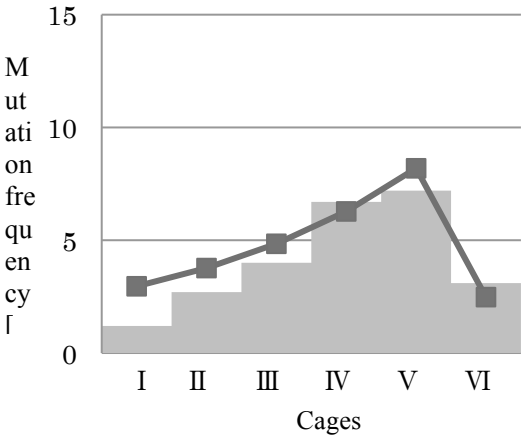

Fig.1 Comparison between experimental data (bar graph) and theoretical value (line graph) for Brood I sample of 6 cages with 0.5 rad/min irradiation.

We could reproduced the data. We found that it is important to take account of the difference in the radiation sensitivity between the germ cells and the spermatogonia cells.

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2) W.L. Russell and E.M. Kelly, Proc. Natl. Acad. Sci. USA 79, 542-544 (1982)
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P02

Two-step model for the occurrence of retinoblastoma

Tetsuhiro Kinugawa[1], Takahiro Wada[1] & Yuichiro Manabe[2]

Kansai University (Japan)[1], Osaka University (Japan)[2]

It is widely accepted that cancerization is caused by the accumulation of gene mutations (Knudson hypothesis [1]). We propose a mathematical model which describes the occurrence of retinoblastoma on the basis of Knudson hypothesis. According to Knudson hypothesis, mutations of both genes called Rb1 are required to develop retinoblastoma. Retinoblastoma can be classified in two categories, hereditary and nonhereditary cases. As hereditary cases already have one mutated Rb1 gene, one mutation of the other Rb1 gene is required, while two mutations are required in nonhereditary cases. Considering this difference between the two categories, we propose a mathematical model named "two-step model", which expresses the sequence of gene mutations required to develop retinoblastoma.

$$dN0/dt = -A0N0 \qquad dN1/dt = A0N0 - A1N1 \quad dN2/dt = A1N1 \tag{1}$$

In equations (1), N_j (j=0,1,2) denote the numbers of cells which have j mutated Rb1 genes. N_2 corresponds to cancer cells. In hereditary cases, cancerization of cells initiates from N_1, while it starts from N_0 in nonhereditary cases. A_j represents the mutation rate from N_j to N_{j+1}.

Using maximum likelihood method, we determined the parameters so as to match the solution of equations (1) to the epidemiological data [2]. Initial values of the N_j are determined by taking account of the frequency of the disease. We also included a term which represents the natural decrease of the cells. The results of the two-step model are shown in Fig. 1 in comparison with the epidemiological data.

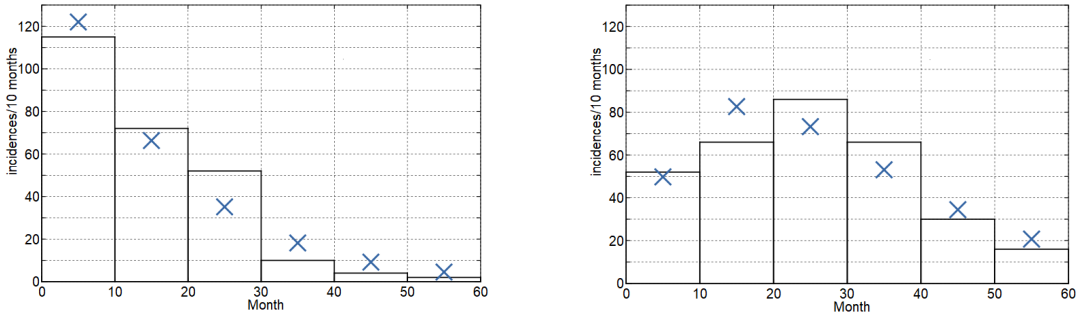

Fig. 1 Comparison between the epidemiological data and the results of the two-step model. Boxes express the epidemiological data, and crosses indicate the results of the two-step model

The two-step model succeeded at representing the qualitative difference between hereditary and nonhereditary cases. However, the two-step model didn't reproduce the peak of the epidemiological data in nonhereditary cases. We will look for more epidemiological data of retinoblastoma so that we can improve our model.

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[1] Knudson, A. G. (1971) *Proc. Natl. Acad. Sci. USA* 68, 820-823

[2] Hethcote, H. W. & Knudson, A. G. (1978) *Proc. Natl. Acad. Sci. USA* 75, 2453-2457

P03

Analysis of Childhood Thyroid Cancer Incidence in Fukushima based on Dose Response Relationship

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Environmental radioactive contamination caused by the Fukushima Dai-ichi Nu-clear Power Plant accident has aroused a great concern regarding a possible in-crease of the incidence of childhood thyroid cancer. The ultrasound examinations conducted as part of Fukushima Health Management Survey (FHMS) provide us with valuable information. FHMS is a key to investigating the health risks caused by low-dose radiation exposure at levels which are estimated to be far lower than those from the Chernobyl accident. FHMS is divided into the preliminary base-line survey (PBLS) and the full-scale survey (FSS), and some of their outcomes are reported regularly and made available to the public. We investigate the dose-response relationship concerning the PBLS and the FSS by using information on the distribution of radioactive Cs isotopes (^{134}Cs and ^{137}Cs) and ^{131}I in soil and also that of air dose rates. Comparison of these results suggests that the behavior of the dose-cancer incidence curve based on the FSS data shows a different structure from that of the PBLS data.

There have been several papers on the incidence of thyroid cancer after the accident, which drew markedly different conclusions regarding an association between incidence of thyroid cancer reported in Fukushima and low-dose radiation exposure. [1] In this paper, we emphasize the importance of investigating the dose-response relationship quantitatively. Fortunately for our purpose, we have detailed deposition maps of gamma-ray emitting radioactive nuclides in eastern Japan based on extensive soil sampling in addition to air dose measurements conducted shortly after the Fukushima accident. [2] We group neighboring municipalities with similar radiation levels so that each area has the child population large enough to contain a meaningful number of thyroid cancer cases. Based on the analysis of both populations and dose distributions, the whole prefecture is divided into six areas. We perform a Poisson regression analysis with a straight line $N = ax + b$ with x being the air-dose rate or the amount of ^{131}I in soil and N being the number of cancer cases per 10^5 people.

The results are summarized as follows.

(1) We found a negative correlation for the thyroid cancer case in the PBLS with the dose distribution. The 95% confidence interval contains the case of no correlation.

(2) We found a positive correlation for the thyroid cancer case in the FSS with the air-dose distribution. The probability of positive correlation in the likelihood distribution is 94.5%.

(3) We found a positive correlation between the thyroid cancer cases in the FSS and the amount of ^{131}I, but the AIC value indicates that this correlation is smaller than that of the air dose rate.

We found a positive correlation between the thyroid cancer case reported in the FSS and the radiation doses, with the association stronger with external exposure than with internal one. It is important to continue the study of the dose-cancer relationship as more data are available.

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Acknowledgements This work was supported by JSPS KAKENHI Grant Numbers JP16H03094, JP16H04637, JP15K12204, JP15K14291

P04

Agendas and Issues of Participatory Dialogues by Junior-High and High School Students from Fukushim Hama-doori and Capital Area

- "Exciting Class 2017" by Junior- and High Students on Thyroid Screening Test - Issues and Results of IWAKI Dialogues –

Tetsuo Sawada[1*], Chieko Nakayama[2], Natsumi Kimura[3], Atsushi Koori[4]
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In response to the results of the incandescence classroom 2016 conducted in Tokyo in December 2016, at the end of April 2017, about 20 students of Iwaki High School and Kanagawa University High School had a dialogue at Iwaki High School with the schedule of an overnight stay. As a result, they derived 20 items in three issues. They are: 1) things I would like to ask the expert (12 items), 2) what I would like to discuss with everyone (4 items), and 3) opinions (4 items).

1. Introduction

In December 2016 in Tokyo, the "Incandescence Classroom 2016", which is a place of participatory dialogue on thyroid inspection conducted for children in the whole area of Fukushima prefecture, with the aim of constructing an authority related to nuclear power and radiation. In response to the participation of high school students at that time, "Iwaki Dialogue -- Incandescent Classroom 2017" was held at Iwaki High School to aim for deepening the dialogue.

2. Issues, methodology, and results

1) Issues and objective

Under the four indicators of Socio-Scientific Issue (SSI) (training of citizens awaiting scientific knowledge, introspective development of social responsibility, intuition and logical discussion, demonstration of critical thinking), we aimed to raise the dialogue capability and create a sprout of collaborative engagement. Also Iwaki Dialogue aimed to visualize issues with publicity through dialogue and lead to advocacy (promotion of public policy formation).

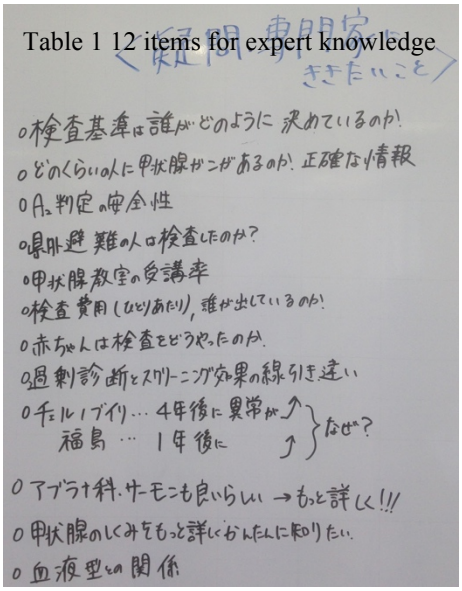
2) Design of opportunity or methodology

According to "incandescence classroom 2016" [1, 2, 3], the dialogue conversation and voluntary facilitation were the major components of the methodology. Two female high school students became the main facilitator, and conducted a dialogue of three sessions over two days.

3) Results

By the two-day dialogue, the question of 12 items shown in Table 1 was summarized. In addition to this, four items which they want to discuss with everyone: 1) the necessity to divide A1, A2, 2) thyroid meal diet - its development, 3) how to disseminate delivery classes, 4) measures to prevent lowering of the examination rate. Four opinions were derived: i) global standards should be set for the thyroid test, ii) thyroid test should be included in conventional health examinations, iii) implementation in other areas, and iv) data comparison with other areas. In 2), there was a sprouting of cooperative engagement.

Table 1 12 items for expert knowledge



3. Conclusion

Based on information sharing and introspective thinking in high school students, high school students gather what they want to know (expertise),

what they want to talk about, and opinions. Next is finally going into the phase of providing expert knowledge.

References: [1-3] AESJ Proc. 2017 Annual mtg., 2C13-15

P05

The development of ESR dosimetry using human hair

S. Hirota, C. Gonzales, H. Yasuda (Hiroshima Univ. RIRBM)

ESR dosimetry has been developed as a method to evaluate dose of victims without dosimeters and some specific organ dose which can't be estimated by other biological dosimetry methods for whole-body dose.

ESR dosimetry measures an amount of radicals which have unpaired electrons induced by radiation in samples. The energy level of atoms or molecules of a sample is split in magnetic field due to Zeeman effect for unpaired electrons. In ESR, microwave absorption of samples is measured as magnetic field is scanned.

Examples of samples for ESR measurement were tooth enamel, sugar of candy in victim's pocket etc. in previous studies [1][2]. Especially handling of tooth enamel for ESR has been established over 1 Gy, but there is a difficulty in sampling due to its highly invasiveness. To solve this problem, other samples, such as nail and hair, with low invasiveness has been tried, but high and unstable background of these samples has been an obstacle for dosimetry.

The background can be removed by washing samples with water, but this treatment has been thought to vanish signals induced by radiation also. However, some previous studies reported that very small signals after water treatment in nail samples [3][4].

Both nails and hairs are made by α-keratin mainly. So, some characteristics of background are common in these samples. In case of hair, melanin is additional source of background.

In this poster, I will report about background measurement of Japanese hairs.

Reference:

[1] Appl. Rad. Isot. (1993) 44:85-90

[2] Appl. Rad. Iso. (2010)68: 2033-2116

[3] Rad. Env. Biophys. (2008) 47:515-526

[4] Rad. Env. Biophys. (2014) 53:291-303

P06

Particle Therapy System Simulation Framework and its application for probing material composition in patient body

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[1]National Institute of Technology, Toyama College; [2]Kyoto Prefectural Univ., Radiology; [3]Tokyo Women's Medical Univ., Medical Physics; [4]Tokai Univ., School of Medicine, Radiation Oncology

The reliable dose control has been so far approached by improving the dose calculation algorithms[1,2]. However, the use of secondary gamma-rays via nuclear interactions inside patient body is of interest for monitoring the irradiation field during the treatment. The project, "Tumor Response Observation System for Dose-volume delivery Guided Particle Therapy, TROS-DGPT", has been developing a hybrid beam online PET and Compton Camera system (HBOLP/CCs)[3] for this purpose. Such gamma rays reflect not only the irradiation field but also the material composition inside patient body. The experimental analysis of positron emitter nuclei production and the treatment site has been firstly reported by Miyatake et al.[4] It used the beam on-line PET system mounted on a rotating gantry port (BOLPs-RGp) at the National Cancer Center, Kashiwa[5]. In this paper, we studied the prompt gamma-ray energy spectra in various material target by using Monte Carlo simulation. We describe about the functions in the Geant4[6] based particle therapy system simulation framework, PTSIM[7-8], and its application for probing the material composition in the target.

The PTSIM is a single application software for simulating interactions of particle with matter. It was originally developed for calculating dose profiles inside patient and validating treatment plans in proton and carbon therapy facilities. The functions were extended according to the updates of treatment techniques including the imaging devices for the irradiation field monitoring.

In this study, the simulation was performed for 190 MeV proton beam with a target in homogeneous material. The size of target was set to 30 cm square and 50 cm depth. The material was chosen from polyethylene (C_2H_2), water (H_2O), acrylic ($C_5H_8O_2$) and a soft tissue material in Geant4 (G4_MUSCLE_WITH_SUCROSE). These materials are categorized as carbon enriched, oxygen enriched or admixture of carbon and oxygen elements with different mass fractions. The gamma-rays generated via nuclear interactions were detected at the simple tabular detector around the target. The energy distributions were compared among the target materials.

Several energy spectra were observed in the energy distributions such as deexcitation states of ^{12}C (4.4MeV), ^{14}C(2.3MeV), ^{15}O(5.2MeV), ^{16}O(6.1MeV, 6.9MeV, 7.1MeV). The results of the correlation between the materials and the spectra are reported at the conference.

Acknowledgements

This work was supported in part by Japan Science Technology Agency (AMED), Development of Advanced Measurement and Analysis Systems (AMED-SENTAN) program.

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3) Nishio T: Innovative proton therapy with irradiated volume image by target nuclear fragment reaction, RIST News No. 50, 24-35, 2011.
4) Miyatake A, Nishio T et al.: Measurement and verification of positron emitter nuclei generated at each treatment site by target nuclear fragment reactions in proton therapy, Medical Physics 37(8), 4445-4455, 2010.
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6) Agostinelli S, Allison J, Amako K, et al.: Geant4 – a simulation toolkit, Nuclear Instruments and Methods, A506(3), 250 -303, 2003.
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P07

Twitter analysis of public response to radiation exposure after the Fukushima Daiichi Nuclear accident

*Kazuko Uno[1], Masaharu Tsubokura[2], Yosuke Onoue[3], Saori Kobayahsi[3], Hitoshi Fujimiya[4], Hiroyuki A. Torii[5] ([1]Louis Pasteur Center for Medical Research, [2]Soma Central Hospital & Minami-soma Municipal General Hospital, [3]Science for Innovation Policy Unit, Center for the Promotion of Interdisciplinary Education and Research, Kyoto University, [4]Dynacom Co., Ltd., [5]School of Science, The University of Tokyo)

In the aftermath of the Fukushima Daiichi nuclear disaster, there was confusion among citizens in Japan about the effects of radiation, due to a flood of contradictory opinions, particularly on social media. Our aim is to identify the source of information and how it spreads on social media so this information can lead to improvements in crisis communication during large-scale disasters. Twitter data was purchased amounting to twenty-five million tweets. Tweet contents were related to radiation in Fukushima and were sent out from March 1st to September 15th, 2011. We analyzed this Twitter data to see if and how tweets influenced public reactions.

The top 100 influencers, the individuals who had the greatest impact on the spread of relevant information, were categorized in three groups based on the contents of their tweets. Group A consisted on influencers whose tweets about radiation were based on relevant scientific evidence; in group B, the majority sent out cautionary messages that over-emphasized or exaggerate the danger of radiation. Group C consisted mostly of influencers who were media related.

Data showed that influencers within each group often retweeted each other. As well, we noted that tweets generated by group B influencers accounted for the majority of retweets one month after the disaster. Group B did not lose its majority share of re-tweets even after six months after the nuclear incident. We speculate that group B maintained its dominance because of the higher number of mutual mentions among the influencers in the group, and we verified this hypothesis using network analysis. Results indicated that the density of connection among the influencers is relevant to the ease with which information spreads. Further research is necessary to understand how to effectively convey scientific but not emotional information through SNS.

Abstracts of High school Special Session

HSS01	Dose rate mapping project by students for the creation of a better future : TEAM YURIKAMOME
HSS02	The special quality of the radiation meter and radiation measurement around the Fukushima Daiichi nuclear power plan : Kitasuma Senior High School, Hyogo
HSS03	Trial of the Discussion about Radiation at Kyoto Girls' High School : Kyoto girls' high school, Kyoto
HSS04	Radiation measurement of stones in historical sites and building materials in Kyoto : Rakunan High School, Kyoto
HSS05	What is the meaning for us to keep on choosing nuclear power plants? : Tokyo Gakugei University International Secondary School, Tokyo
HSS06	The Investigation of the Decontamination Methods and the Impression of Fukushima from Overseas : Adachi High School, Fukushima
HSS07	Expanding for Cooling Area Range of Peltier Cooling Type Cloud Chamber : Adachi high school, Fukushima
HSS08	The Changes in Harmful Rumors about Fukushima in the Newspapers immediately after Fukushima Daiichi Nuclear Disaster in 2011. : Adachi High School, Fukushima
HSS09	Individual dose measurement by using D-shuttle: the study of values of outliers measured in the dosimeter and the discussion of dose restriction : Fukushima High School, Fukushima

HSS01

Dose rate mapping project by students for the creation of a better future.

TEAM YURIKAMOME

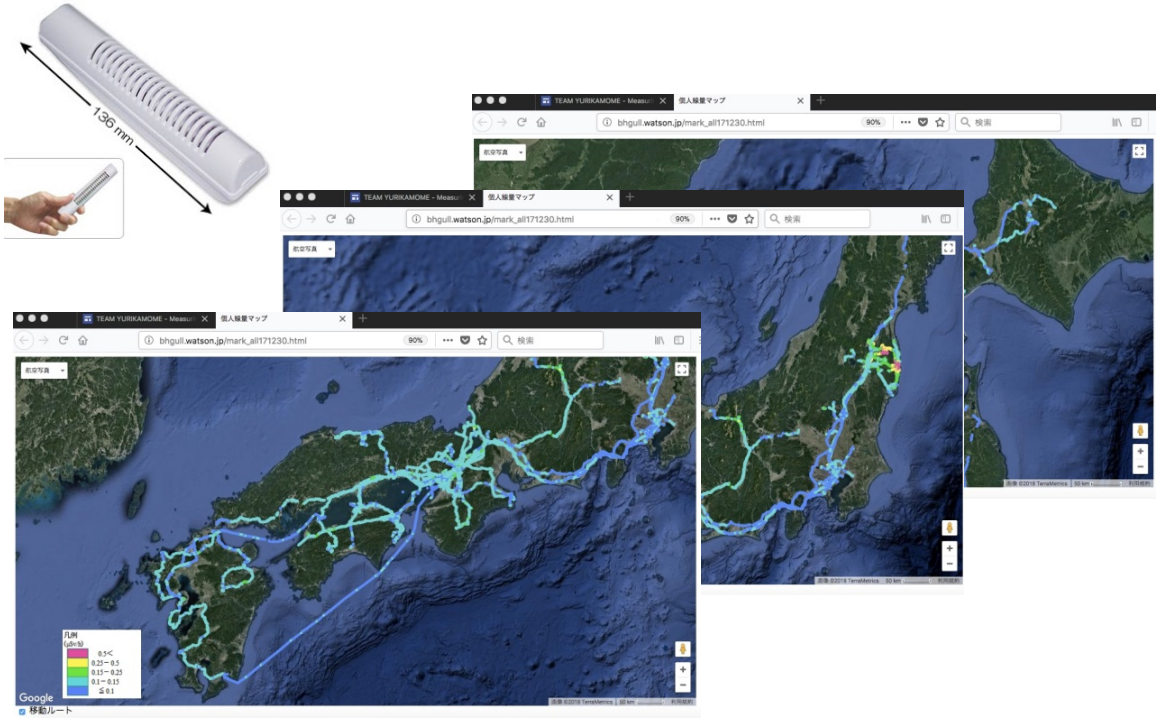
Imagine a bowl of hot water of 80 degrees centigrade placed just in front of you. You would feel the steam and heat; and you would instantly judge that you must not carelessly touch it. This judgement of yours is derived from your experiences, not by your pure instinct. You learn the danger of hot water as a child through your body experiences: water could be hot or cold, and it could burn you when it is too hot; and the burning could be serious. And also we have, in our daily lives, many opportunities to measure temperatures of our bodies as well as of water with thermometers. Our learning through experiences enables us to immediately see the danger of boiling water.

We would suggest that the same experience-based learning should be applicable to our learning of radiation. Last year, the radiation-mapping project by pupils at elementary school and students at junior and senior high school: “TEAM YURIKAMOME [Black-headed Gull]” have started with this idea.

TEAM YURIKAMOME website:

Japanese: https://sites.google.com/view/yurikamome/

English: https://sites.google.com/view/bhgull/



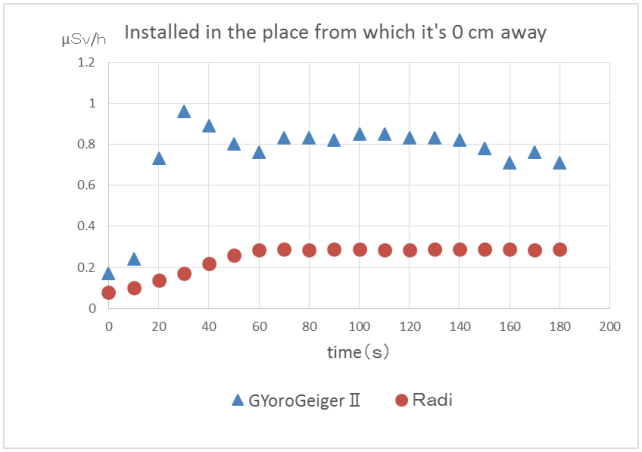
HSS02

The special quality of the radiation meter and radiation measurement around the Fukushima Daiichi nuclear power plant

Sako Tatsuki, Taysuki Ito, Hiroyasu Tsuboi (Kitasuma Senior High School)

By comparing the precision of measuring and response between GYoroGeigerⅡ (Geiger Muller's canal system) and RADI (Scintillation system), we found the special qualities of each measuring machine and considered the possible problems that could arise when measuring.

(1) We installed a Radium ceramic ball and placed it at 0, 4, 8, 12 cm away from the two measuring machines and measured every 10 seconds.



(fig. 1－1)

(fig 1－2)

(2) We measured the radiation dose around the Fukushima Daiichi nuclear power plant and did a mapping. We measured it with a car while moving but stopped by Iitate, Namie, MinamiSoma.

(fig. 2－1)

HSS03

Trial of the Discussion about Radiation at Kyoto Girls' High School

ISHIDA Akari, KATAOKA Ami, KUBOTA Saki,
OOTSUKA Akane, OKUMURA Erika,
OKUMURA Sayaka, TORII Chitose
Kyoto girls' high school

1. Introduction

What is "radiation"? It is difficult for us to think about radiation problem because we don't know well about radiation and we have an image that radiation is something horrible.

But discussing social problems with each other must be meaningful for us. So, we had the discussion program to think about radiation problems. We report how we discussed and how we felt.

2. Method

About 80 students of Kyoto girls' high school took part in the discussion. In advance eight members of them including us looked into two themes. One is "Do you receive radiation treatment?" The other is "Do you continue to use nuclear power plants?"

We presented both favorable and unfavorable opinions and evidence. After hearing about the opinions, all of the students discussed how they think.

3. Result

We have a discussion on 15th March, so we don't know how the trial result now. We will be able to report the result on BER 2018. Please look forward to our report!

The look of discussion of the past (2013)

HSS04

Radiation measurement of stones in historical sites and building materials in Kyoto

Rena MIYAOKA[†], Yuichi TSUNOYAMA[§]

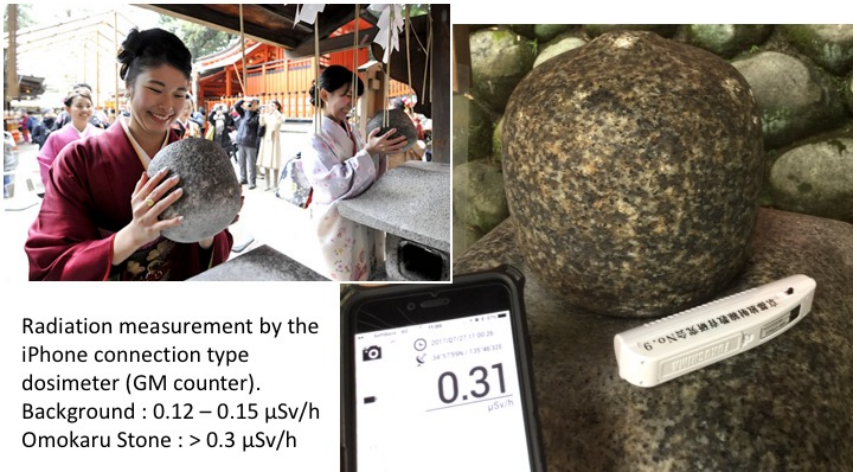
[†]Rakunan High School, [§]Radioisotope research center, Kyoto University

It is well known that radiation dose emitted from stones varies depending on the amount of radioisotopes and radioactive nuclear species contained in the ore. In our city “Kyoto”, There are famous temples and shrines built in hundreds of years ago. In such historical places, stone statues for people's beliefs are often built. We have measured the radiation dose rate in the immediate vicinity of some of those stones. Interestingly, in some stone statues, the dose rate was several times higher than the background (Fig.1). From ancient times, Japanese may have been praying of stones which radiation is slightly higher as object of faith ☺

Our results of measurement will be reported.

Fig.1 Omokaru Stone at Fushimi Inari shrine in Kyoto.

There are two rounded stones that are placed on top of a stone-lantern for you to lift up. Before lifting one up you make a wish, then when you lift the stone up, if it seems lighter than you imagined it would be, then the wish will come true but if it seems heavier than you imagined it would be, then the wish will not be realized.



Radiation measurement by the iPhone connection type dosimeter (GM counter).
Background : 0.12 – 0.15 μSv/h
Omokaru Stone : > 0.3 μSv/h

HSS05

What is the meaning for us to keep on choosing nuclear power plants?

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Before the Fukushima daiichi nuclear disaster that happened around 7 years ago, 30% of Japan's electricity was generated by nuclear power plants. Currently, that number has been kept low to approximately 2%, but there are still arguments both for and against. We have been investigating the reality of nuclear power plants and analyzing the views of people with different perspectives in order to understand why Japan has kept on choosing nuclear power plants. Our final goal is to stop the harm the nuclear power plants bring on people and to create a society that chooses its energy source more responsibly, while understanding the flaws of nuclear power plants. The premise is that if we are using electricity that is generated by nuclear power plants, we are "choosing" to use them. However, the reality is that we do not have enough decent information about this situation and that we, as individuals, aren't aware that we are "choosing". Thus, this year we analyzed the situation of nuclear power plants by interviewing people with different points of view, and sought to find an effective way to present this situation and actually presented as well. Through the results of the survey we took from students before and after the presentation by the filmmaker Hitomi Kamanaka, interviews from a variety of people, and our research on this problem from a scientific point of view, we are finding out that we are choosing to use nuclear power with limited knowledge and little consideration.

HSS06

The Investigation of the Decontamination Methods and the Impression of Fukushima from Overseas

Yuka Shinotsuka[1], Shinya Ishii[1]

[1]Fukushima Prefectural Adachi High School

The leading clean up program of radioactive contaminated area of Fukushima is decontamination, which is to remove the surface of the soil with radioactive cesium. Generally, the scrapped soil is buried underground and covered with no contaminated soil, because the air does rate due to radioactive substances such as radioactive cesium decreases by shielded by the soil. I confirmed the fact by experiment. First, the radiation source which is mantle of camping lights lanterns was laid down on the bottom of a plastic container whose depth is about 5 cm and I measured the air does rate by gyorogeiger which is GM counter around the top of the container. Next, plastic bag which was packing the no contaminated soil and whose height was about 4 cm. The plastic bag was put on the radiation source, and I measured the air does rate again around the same point. The air does rate changed from 0.51 μSv/h to 0.24 μSv/h. The contaminated school ground has been buried at the range from 150cm to 90cm underground. Because of he decreasing effect of the air does rate by the shielding the soil and by taking a distance from contaminated soil, the air does rate of the ground is about 0.11 μSv/h today.

I made a presentation about this at the Environment Creation Symposium on March. The words that were told from overseas at the time of the symposium remained impressive. He said that he was asked, “Can people lice in Fukushima?” in USA. It was not only a shock for me, but also what made me think at that time. Now, I have investigated the impression of Fukushima from overseas by the Internet. I’d like to discuss this, too.

HSS07

Expanding for Cooling Area Range of Peltier Cooling Type Cloud Chamber

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Fukushima Prefectural Adachi high school

Through our activities to convey the current situation of the Fukushima Prefecture and to interact with students from other prefectures, I learned that few people feel there is radiation in everywhere, not only in Fukushima and have the perception that the whole area of Fukushima prefecture is safe. To change this situation, we would like to inform that there is natural radiation everywhere, as a first step. To achieve it, we guess a cloud chamber that we can observe natural radiation is effective. We want to demonstrate the experiment of the cloud chamber and compare between Fukushima and other area.

So far, we have made a cloud chamber using Peltier and CPU cooler in order to improve portability and convenience. However, we can hardly observe natural radiation, because the cooling area range of Peltier elements is narrow, only 16 cm^2. So we have been trying to expanding by using copper plate and increasing the number of Peltier elements.

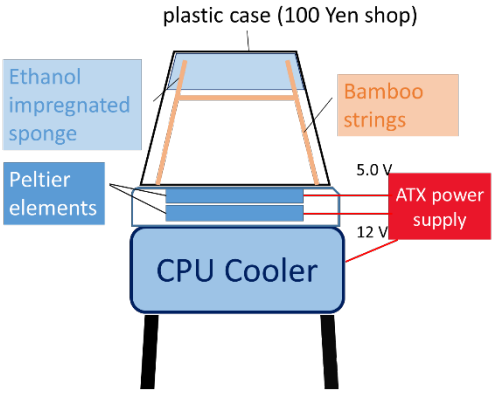

Fig.1. System of the Peltier cooling type cloud chamber.

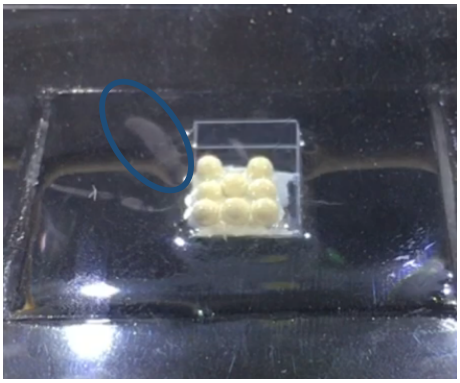

Fig.2. Alpha-rays track observed by our system. The source is monazite ore.

HSS08

The Changes in Harmful Rumors about Fukushima in the Newspapers immediately after Fukushima Daiichi Nuclear Disaster in 2011.

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It has been 7 years since Fukushima Daiichi nuclear accident this year, harmful rumors about Fukushima still remain almost as the same as 7 years ago. I hope that harmful rumors will never be heard if a similar accident occurs. In order to suggest effective means to do it, as a first step, I'd like to introduce you some types of harmful rumors from newspaper articles in those days. At first, I used to define harmful rumors were only related to economic damages but I gradually noticed there were some kinds of harmful rumors. For example, bullying to evacuated children from Fukushima and boycotts vegetables or fruits from Fukushima. Especially, the harmful rumors just after the accident, I am interested in, effected directly to the life of victims. One example, doctors' support team from Tokyo heading for Miharu town in Fukushima changed its destination into Miyagi prefecture because of the fear about the nuclear accident, reported on the newspaper on March 20. In fact, Miharu town was far more than 40 km away from the crippled Fukushima Daiichi Nuclear Power Plant, but they judged Miharu was dangerous to go in.

Through the newspaper articles I would like to discuss the factors of the harmful rumors.


4号機の新たな写真公開 電

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Fig.1. The newspaper article about harmful rumors on March 2011 .

HSS09

Individual dose measurement by using D-shuttle: the study of values of outliers measured in the dosimeter and the discussion of dose restriction

Fukushima High School:
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Abstract

Since 2014, after the Fukushima Daiichi Nuclear Accident, we have conducted the measurement of individual radiation dose by using a dosimeter called D-shuttle, by which we compared the data of people inside Fukushima, outside Fukushima and overseas. Even though the result shows that dose rate of people in Fukushima is as low as that of people outside Fukushima and overseas, the values of high-dose "outliers" measured in the measurement are not clear, which we could find out one of the causes of such "outliers." Also, during the measurement, we have found that the values of individual dose measured with D-shuttle are quite smaller than we expected. Comparing the data, we have realized that the dose restriction value designated by the government, 0.23 μ Sv/h (a calculated value based on the restriction by the ICRP's Recommendation, 1mSv/y) is an overestimated one, by which the decisions of decontamination work in some municipalities were made, and cost a lot.

1. Objective

- To find out what causes the values of high-dose "outliers" in the D-shuttle measurement
- To compare dose rate measured by air dose monitoring with individual dose measured by D-shuttle

2. Method

- To check whether anti-shoplifting sensors have some effects on the data of D-shuttle
- To compare the data of air dose and individual dose in the same conditions such as place or time

3. Result

- One of the causes of the values of high-dose "outliers" is the reaction to anti-shoplifting sensors
- Individual dose of people in Fukushima is as low as that of people outside Fukushima and overseas, and the values of individual dose measured with D-shuttle are quite smaller than we expected

4. Discussion

- The result that the values of high-dose "outliers" are caused by anti-shoplift sensors confirms that the individual dose collected in the D-shuttle measurement in Fukushima is as low as that of other areas, and also that the Fukushima Daiichi Nuclear accident did not affect the individual dose of people in Fukushima seriously.

- The other result that the values of individual dose measured with D-shuttle are quite smaller than we expected implies the decisions made by the government should be based on individual dose in the case of nuclear disasters, as the Fukushima's case shows the over-estimate of the dose, by which some social problems were caused.

5. Conclusion

- The individual dose in Fukushima we measured after the Fukushima Daiichi Nuclear accident is much smaller than we expected. Judging from this data, the designated value by the Japanese government, 0.23 μ Sv/h (based on the ICRP's Recommendation), is an overestimated one, considering resulting social problems such as the high cost of decontamination work or the collapse of communities. This should be one of the lessons to be learnt from the Fukushima's case.

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