### Priority Subjects — Establishment of Optimal Risk Management

## Quantitative Evaluation of Low-Dose Radiation Risk and its Reflection on Radiation Protection

### Background and Objective

The radiation exposure to workers in nuclear facilities, and to the public from environmental contamination caused by nuclear accidents are characterized as prolonged low-dose-rate exposures. Epidemiological research studies of residents in high background radiation areas suggest the existence of a dose-rate effect with no increase in radiation risks at a low-dose-rate, unlike the high-dose-rate radiation exposure. Understanding biological mechanisms of the doserate effect could contribute to the establishment of reasonable protection criteria, and relieve public concern towards radiation exposure. Furthermore, the accuracy of dose evaluation underlying radiation risk assessment is also an important issue.

This project aims to reflect the dose-rate effect in radiation protection systems by elucidating its biological mechanisms through experimental studies, and to develop dose evaluation methods to reduce uncertainties in radiation risk assessment.

#### Main results

# Developing an experimental system for radiation effect on tissue stem cell to elucidate mechanisms of the dose-rate effect

Cancer is considered to be initiated by an accumulation of lesions in tissue stem cells (TSC<sup>\*1</sup>). TSCs in normal tissues maintain their function in groups (TSC pools). In the case of low-dose-rate radiation exposure, damaged and undamaged TSCs would be intermingled in TSC pools. If damaged TSCs can be excluded by competition between damaged and non-damaged TSCs, it can be assumed that lesions in TSCs caused by radiation would accumulate less in TSC pools at low dose-rate exposure. We tackle explorations to confirm this hypothesis, in which these mechanisms could explain the dose-rate effect.

To study the competition in detail, we developed a novel *in vitro* assay using organoid<sup>\*2</sup> formation from intestinal TSCs (Fig. 1) and showed the number of organoids as an index of survival rates of TSCs after 0-4 Gy exposure (Fig. 2 left). By using this system, we quantitatively clarified that organoid-forming TSCs irradiated with X-rays at doses  $\geq$  2 Gy acquired increased organoid-regenerating capacity (Fig. 2 right). Thus we demonstrated that the *in vitro* assay can quantitatively analyze behaviors of intestinal TSCs after radiation exposure and it is useful to verify the dose-rate effect by competition between TSCs<sup>[1]</sup>.

# 2 Estimating aging characteristics of radiation-counting efficiency for clearance inspection\*<sup>3</sup>

In the case of clearance inspection for materials used at nuclear facilities, it is necessary to estimate low level radioactivity, so enhancement of the precision of radioactivity estimation is an important issue. One important factor of estimating low level radioactivity is the effect of corrosion products generated on alloys due to aging. If radiations are shielded by corrosion products, it is necessary to evaluate the effect of corrosion products for radiation measurement to avoid underestimation of contamination.

In this study, acceleration tests of corrosion products growth were performed using carbon steel and stainless steel coupon specimens which were contaminated with either <sup>241</sup>Am or <sup>60</sup>Co.

The relationship between amount of corrosion products and decrease of radiation-counting efficiency was obtained (Fig. 3). In order to investigate the growth of corrosion products on alloys in an actual warehouse environment, coupon specimens were placed in warehouses of nuclear facilities for over one year (Fig. 4). These results made it possible to estimate the decrease of radiation-counting efficiency in an actual warehouse environment. For waste contaminated with uranium, we also made the appropriate estimation available for uncertainties due to aging characteristics, taking into account the difference of the alpha particle energy between <sup>241</sup>Am and <sup>238</sup>U <sup>[2, 3]</sup>.

<sup>\*1</sup> Cells which tissue-forming cells originate in. They are also considered as origins of cancer because of their proliferative characters.

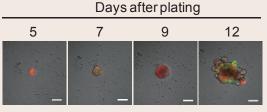
<sup>\*2</sup> Three-dimensional structure of several kinds of functional cells derived from TSCs which shows a cell arrangement similar to living organisms. \*3 Confirmation of radioactivity concentration of materials with radioactivity concentrations below the level which requires treatment as a

radioactive material.

<sup>[1]</sup> YAMAUCHI, M. et al., J Radiat Res, 55(2), 381-390 (2014).

<sup>[2]</sup> ICHIJI, T. and KAWAMURA, H. Jpn. J. Health Phys. 48(4), 171-179 (2013).

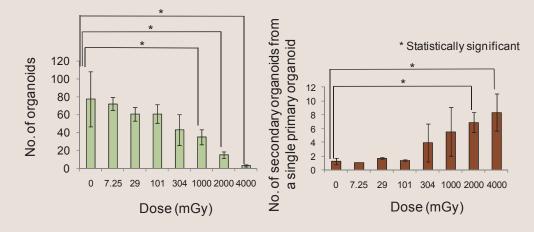
<sup>[3]</sup> ICHIJI, T. and KAWAMURA, H. Jpn. J. Health Phys. 48(4), 200-205 (2013).



Green: TSCs Red: Functional cells differentiated from TSCs

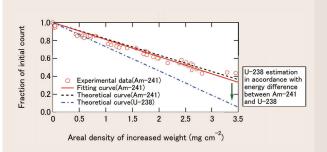
### Fig. 1: Organoid formation from intestinal TSCs

Pictures of organoids formed *in vitro* from intestinal cells containing TSCs isolated from mice intestines. The green color represents TSCs while the red color indicates cells derives from TSCs. Projections similar to crypts which exist in the roots of villi in small intestine were formed after 12 days of culture. At the bottom of the projections, green cells, which represent TSCs, were observed, in a similar manner to the distribution *in vivo*.



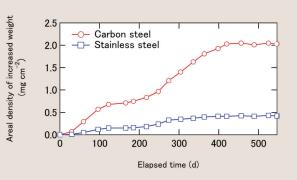
### Fig. 2: Assessment of radiation effects using the organoid assay

The number of organoids after radiation exposure was observed (left). Because each organoid is formed from a single TSC, the efficiency of organoid formation represents a survival rate of TSCs after exposure. Significant decrease was observed after 1 Gy (1000 mGy) compared with non-irradiated control. There have been no quantitative data on the tissue-regenerating capacity of surviving TSCs for the repair of wounded tissues after radiation exposure. Then, the primary organoids formed in the experiments shown at the left were dissociated and they were passaged to allow secondary organoid formation to assess organoid-regenerating capacity (right). The number of secondary organoids produced from a single primary organoid was measured, and quantitatively clarified to increase with radiation dose.



#### Fig. 3: Decrease in radiation-counting efficiency caused by corrosion products on alloy (experimental data and theoretical values)

This figure shows the result of the decrease in radiationcounting efficiency of carbon steel samples, where <sup>241</sup>Am was dropped. Experimental data show good agreement with the theoretical values. Using the theoretical curve which was calculated taking into account the difference of the alpha particle energy between <sup>241</sup>Am and <sup>238</sup>U, it will be possible to estimate the decrease for <sup>238</sup>U in the radiation-counting efficiency caused by corrosion products.



## Fig. 4: Amount of corrosion products on alloys placed in the warehouse environment at the nuclear facility

Carbon steel and stainless steel coupon specimens were placed in a warehouse environment at a nuclear facility and the amount of corrosion products generated on coupon specimens was measured. Using the data illustrated in Fig. 3, it is assumed that radiation-counting efficiency may drop to 40-50% of the initial value for carbon steel, which was contaminated by  $^{238}$ U and elapsed over 500 days.