Dose-rate effects on cancer mortality risk estimates for Japanese nuclear workers

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BACKGROUND

The Institute of Radiation Epidemiology, Radiation Effects Association (REA) has been conducting the Japanese Epidemiological Study of Low-Dose Radiation Effects (J-EPISODE) in nuclear industry workers since 1990, with a view to clarifying the low-dose radiation risk by compiling individual recorded doses, following up vital status, and ascertaining the cause of death. The fifth analysis report, based on the follow up until 2010, indicated that smoking might be a strong confounder in the association with radiation and all-cancer mortality, and the report therefore had no clear conclusion regarding low-dose radiation risk.

The LNT model used with atomic bomb survivors with high dose rates and acute irradiation was not compatible with the results of J-EPISODE. Conversely, the knowledge of biology indicated recovery effects for gene damage induced by radiation exposure, which might contribute to the differences in radiation effects among these two cohorts with greatly differing dose rates.

The annual mean dose of J-EPISODE exceeded 3.5mSv in the late 1970s; however, the dose reduction measures taken subsequently resulted in a sharp decline to below 1mSv, or less than environmental radiation. The mean cumulative dose was 14mSv at the end of follow up.

ANALYSIS METHOD

We investigated the dose rate effects on mortality risk from low dose and low dose rate radiation exposure. The study subjects were 34,976 employees of power companies, who were selected from among the 204,103 participants in the fifth analysis to provide uniform characteristics other than dose. The endpoint was cancer mortality, excluding leukaemia. The individual annual recorded dose was supplied by the Radiation Dose Registry Center, REA.

The dose rate was defined using the annual dose as a proxy index, and the maximum annual dose was used as the dose rate in the present analysis.

The results for logistics analysis at the end of follow up demonstrated that the death rate was more affected by the dose rate than by the cumulative dose. We also tested the goodness of fit between the LNT models estimated by Poisson regression, using the cumulative dose or the dose rate as time dependent variables, and analyzed the dose rate effects on the excess relative risk in relation to the cumulative dose.

Keywords: occupational cohort study, cancer mortality, dose rate

(2,300 characters, excluding titles, authors and authors' affiliation)

J-EPISODE (Japanese Epidemiological Study of Low-Dose Radiation Effects)

Testing the assumptions of the LNT model

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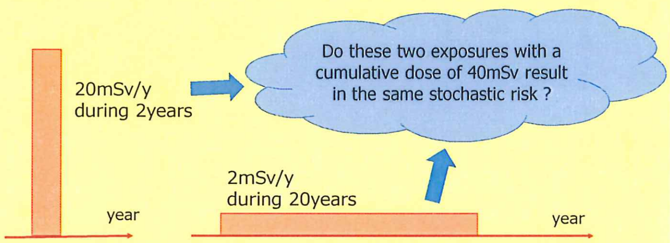
Objectives of the present study

✓ The LNT model is based on the assumption that the excess risk is proportional to the cumulative exposed dose, regardless of the annual rate of exposed doses.

✓ The aim is to verify whether the assumption is valid by using a time window approach.



Trends of dose exposures in Japan

✓ Most nuclear workers have engaged in NPPs.

✓ Commercial NPPs have been in operation since 1966.

✓ The annual exposure dose at the 95th percentile was over 10mSv/y in the 1970s, but declined sharply, to less than the natural radiation level (Fig. 1).

✓ The dose exposed during 1970–85 largely affected the cumulative dose during the follow-up period of 1991–2010, and consequently might be associated with cancer mortality.

Methods and results:
Two dose-rate windows approach to identify dose rate effects

- Lagged cumulative doses were distributed into two windows, depending on the annual dose rate (See Table 1).

$$d(y) = dL(y) + dH(y), \quad d_L(y) = \sum_t^y dr(t)\cdot(dr(t) < x), \quad d_H(y) = \sum_t^y dr(t)\cdot(dr(t) \geq x)$$

where y: year and x: cut point dose rate

- Applied Poisson regression using an additive ERR model;
$\lambda=\lambda_0(age, calendar\ year, region)*(1+\beta_H*d_H+\beta_L*d_L)$

- Tested whether β_H and β_L are identical by changing cut point x from 2 to 20mSv/year.

- The results revealed that the estimates of β_L were negative, while x<10mSv/year, and smaller than β_H below 20mSv /year (Fig. 2).

Table 1 Illustration of two dose-rate windows

(For instance: cut point x=5mSv/year)

Year		1971	72	73	74	75	76	77	78
Annual dose exposed (mSv)	dr(y)	1	3	6	10	8	6	4	2
Annual dose < 5mSv		1	3					4	2
Annual dose >= 5mSv				6	10	8	6		
Cumulative dose (mSv)	d(y)	1	4	10	20	28	34	38	40
Cumulative dose received at annual dose rate < 5mSv/year	$d_L(y)$	1	4	4	4	4	4	8	10
Cumulative dose received at annual dose rate >= 5mSv/year	$d_H(y)$	0	0	6	16	24	30	30	30

Profile of the present study cohort

Follow-up period: 1991–2010

Size: 204,103 male nuclear workers

Mean age at the end: 55.6 years old

Total follow-up: 2.89 million person-years

Mean follow-up: 14.2 years/person

Mean cumulative dose: 9.4 mSv at the beginning
13.8 mSv the end

All death: 20,519

Caused by cancer, excluding leukemia: 7,929

Fig. 1 Trends of mean cumulative dose and annual dose at the 95th percentile for those who started radiation work since 1970, 1980, and 1990, respectively (N=204,103)

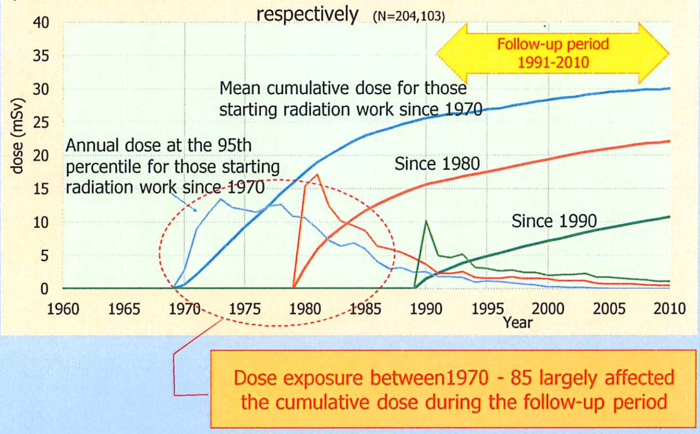
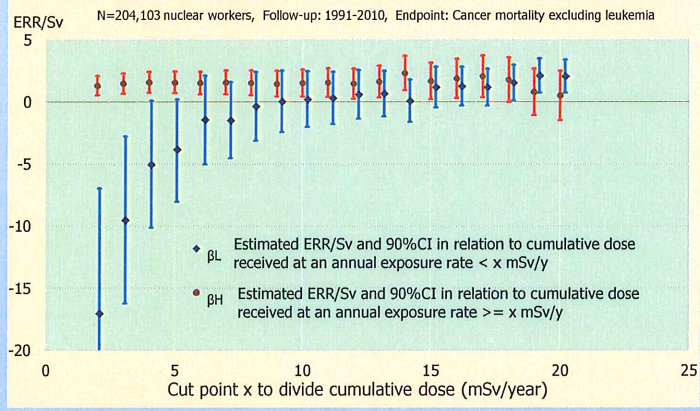


Fig. 2 Results of Dose-rate Windows Approach by Changing Windows



Conclusions

✓ A cumulative dose derived from an extremely low annual dose rate suggests a different dose response than that from a higher dose rate.

✓ We propose paying attention not only to cumulative doses, but also to the exposure dose rate and duration of exposure.

✓ TO DO: it is necessary to consider the effects of confounders such as smoking.

http://www.rea.or.jp/ire/english/

This study was funded by the Nuclear Regulation Authority of the Government of Japan.