Radioadaptive Responses Induced in Human Lymphocytes of the Inhabitants of Very High Level Natural Radiation Areas in Ramsar, Iran

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Abstract

Background: Ramsar, a city in northern Iran has among the highest levels of natural radiation known to exist in an inhabited area. The high levels of natural radiation in Ramsar prompted us to assess the radioadaptive response of some of the residents with high cumulative doses. We report the effect of cumulative lifetime dose on the coefficient of radioadaptive response.

Methods: Twenty two residents of high level natural radiation areas and thirty three residents from an adjacent normal level natural radiation area participated in this study. In the 1st phase of the experiment 15 healthy residents from high level natural radiation areas and 30 healthy inhabitants of a nearby normal level natural radiation area were studied. After description of the study and its objectives to the participants, they were asked to complete questionnaires, participate in interviews, allow radiation measurements of their homes, and to submit blood samples. In the 2nd phase, seven healthy residents with cumulative lifetime doses of up to 10 Sv were studied for assessing the induction of adaptive response in each study participant and obtaining complementary data. Cultured cells were given a challenge dose of either 2 Gy (1st phase of the study) or 1.5 Gy (2nd phase of the study) of Co-60 gamma radiation.

Results: Overall data showed a significant radioadaptive response in the residents of high level natural radiation areas. Results obtained in the 2nd phase of the study, showed that five out of seven inhabitants exhibited a reduction in induced chromosomal aberrations following exposure to a 1.5 Gy challenge dose of gamma radiation. However, the response in 2 residents with much higher cumulative doses than the others was not statistically different than that of the control population. Regression analysis suggests a linear relationship between the radioadaptive response and cumulative gamma radiation doses up to 1 Gy.

Conclusion: High levels of natural radiation may induce significant adaptive responses in the inhabitants. As the cumulative dose increased from a few hundred mGy to 1 Gy, the magnitude of the induced adaptive response increased linearly. Further research is needed to clarify if decreased radiation susceptibility in the residents of high level natural radiation areas can influence radiogenic risk and this phenomenon may be considered as a potential beneficial effect of high levels of natural radiation.

1. Introduction

Animals and plants have been exposed to natural radiation since the evolution of life on Earth. Life evolved in a radiation field that was much more intense than today (Jaworowski 1997, Karam and Leslie, 1999) and levels of natural radiation vary greatly over the Earth. Ramsar, a northern coastal city in Iran (Fig. 1), has areas with some of the highest levels of natural radiation measured to date. The annual effective dose (excluding radon progeny contributions) in high level natural radiation areas (HLNRAs) of Ramsar is a few times higher than the ICRP-recommended annual effective dose limit for radiation workers. Some inhabitants receive annual doses over 130 mGy yr^{-1} from external terrestrial sources. The HLNRAs of Ramsar are due to ^{226}Ra and its decay products, which have been brought to the surface by the waters of hot springs. There are at least 9 hot springs with different concentrations of radium in Ramsar that are used as spas by both tourists and residents. Due to levels of natural radiation in these areas, up to 200 times higher than normal level natural radiation areas (NLNRAs), some radiation experts have suggested that dwellings having such high levels of natural radiation need remedial actions (Sohrabi 1997). In spite of this, nearly all inhabitants still live in their unaltered paternal dwellings.

Many radiation advisory bodies and regulatory agencies assume that any exposure to radiation carries some degree of risk. This assumption has been contested by many radiation scientists. This paper reports on evidence for a protective radioadaptive response caused by the high natural radiation doses to some residents of Ramsar, Iran. The induction of adaptive response was first reported by Samson and Cairns (1977) in *Escherichia coli.* Chromosome aberrations caused in peripheral blood lymphocytes serve as the best biological indicator of the exposure to ionizing radiation (Hayata *et al.* 1992). The induction of the cytogenetic radioadaptive response in human lymphocytes by low doses of ionizing radiation was first reported by Olivieri *et al.* (1984). They reported that the frequency of chromatid aberrations was down to 50% less than they expected after exposure to 1.5 Gy of x-rays.

Many articles have demonstrated radioadaptive response in plant cells (Cortes et al. 1990), insects (Fritz-Niggli and Schaeppi-Buechi 1991), Chinese hamster V79 cells (Ikushima 1987, 1989a, 1989b), cultured human lymphocytes (Wiencke et al. 1986, Shadley and Wolff 1987, Wolff et al. 1988, Shadley and Wiencke 1989, Sankaranaryanan *et al.* 1989), human embryonic and HeLa cells (Ishii and Watanabe 1996), cultured lymphocytes from occupationally exposed persons (Barquinero *et al.* 1995, Gourabi and Mozdarani 1998), cultured animal lymphocytes (Flores *et al.* 1996), and *in vivo* studies on laboratory animals (Wojcik and Tuschl 1990, Cai and Liu 1990, Farooqi and Kesavan 1993, Liu *et al.* 1992).

There are also reports indicating lack of radioadaptive response in cultured human lymphocytes (Bosi and Olivieri 1989, Olivieri and Bosi 1990, Hain et al. 1992). However, long-term follow up studies indicate that lack of radioadaptive response is not a temporary effect (Mortazavi *et al.* 1999) and in contrast with the early reports of Olivieri and Bosi (1990) does not depend on transient physiological factors (Mortazavi *et al.* 2000, Ikushima and Mortazavi 2000). It has been recently reported that adaptive response studies may have implications in manned deep space journeys. Mortazavi *et al.* proposed that individuals who failed to show an adaptive response in ground-based *in vitro* studies, would not be good candidates for space travel (Mortazavi *et al.* 2003).

Mortazavi *et al.* previously reported preliminary results of their cytogenetical,

immunological and hematological studies on the residents of VHLNRAs of Ramsar (Mortazavi *et al.* 2002a, Ghiassi-Nejad *et al.* 2002, and Mortazavi *et al.* 2002b) suggesting that exposure to high levels of natural background radiation can induce radioadaptive response in human cells. Lymphocytes of Ramsar residents when subjected to 1.5 Gy of gamma rays showed fewer induced chromosome aberrations compared to residents in a nearby normal background control area whose lymphocytes were subjected to the same radiation dose. In this paper we report the effect of cumulative dose on the radioadaptive response.

2. Materials and Methods

2.1. Cell Culture

In the 1st phase of the study, venous blood samples were taken from 15 and 30 healthy volunteers of both sexes who lived in HLNRAs and NLNRAs respectively. The maximum measured dose rate of natural radiation was 155 μSv h^{-1}. In the 2nd phase, seven healthy volunteers from HLNRAs and five healthy volunteers from a nearby NLNRAs with dose rates from 0.07 to 0.11 μSv h^{-1} served as controls. It should be noted that in the 2nd phase, due to our selection criteria for study participants (inhabitants who received the annual doses higher than 300 mSv), only limited number of volunteers from HLNRAs were available for this study. All participants were non-smokers with no alcohol or drug consumption, history of medical irradiation or viral infections. Standard conditions for cell cultivation, irradiation and analysis of chromosome aberrations were used (Ikushima and Mortazavi 2000). Separate cultures were made from each blood sample, using 0.3 ml blood in 4.7 ml Ham's F10 medium (Gibco), supplemented with 20% fetal calf serum (FCS Gibco), 100 U/ml penicillin, 100 μg/ml streptomycin, 1.0% L-glutamine and 1.0% phytohemagglutinin (PHA, Gibco) for mitogenic stimulation. The lymphocytes were incubated in the dark at 37°C for 48 hours after PHA stimulation

2.2. Irradiation

Following this incubation, cells were given a challenge dose of either 2 Gy or 1.5 Gy of Co-60 gamma radiation at a dose rate of 114 mGy/sec. Some of the culture flasks were sham irradiated to assess either the frequency of chromosomal aberrations induced by natural radiation alone in HLNRAs' residents and the spontaneous frequency of aberrations in NLNRA residents. After the challenge dose all the culture flasks were incubated a further either 2 (1st phase) or 6 (2nd phase) hours. Colcemid was added 2 hours before the end of this incubation at a final concentration of 0.25 μg/ml to arrest the dividing lymphocytes at metaphase.

2.3. Slide Preparation

After the two or six hour incubation, the cells were exposed to 0.075 M KCl for 10 min at 37°C and fixed with methanol-acetic acid (3:1 *v*/v). The fixed cells were dropped onto wet slides, air dried and stained with Giemsa. For each data point, about 200 well-spread metaphases were blind scored for chromosomal aberrations. The number of chromatid-type aberrations was determined. Gaps (achromatic lesions smaller than the width of a chromatid) were included in the statistical analysis of the 1st phase but in order to enhance the reliability of the results, these lesions were excluded in the statistical analysis of the 2nd phase.

2.4. Data Analysis

Our basic measurement was the mean chromosomal aberration per cell (MCA). MCA_H indicates cells from a HLNRA and MCA_N indicates cells from a NLNRA. If a challenge dose of 2 or 1.5 Gy was given, this is indicated by "+CD". If no challenge dose was given, it is indicated by "+0". We expect a challenge dose to produce an increase in MCA from both the HLNRA and the NLNRA subjects. If the high background dose does not function as a priming dose, we define the "expected MCA" for subjects from high background areas, MCA_{HE} as:

$$MCA_{HE} = MCA_{H+0} + (MCA_{N+CD} - MCA_{N+0}) \quad (1)$$

Standard error of the MCA_{HE} was calculated according the equation:

$$SE_{MCAHE} = [(SE_{MCA\ H+0})^2 + (SE_{MCA\ N+CD})^2 + (SE_{MCA\ N+0})^2]^{1/2} \quad (2)$$

The coefficient of induced adaptive response (k) in each experiment was calculated as follows:

$$k = MCA_{H+CD} / MCA_{HE} \quad (3)$$

Standard error of the k was calculated according the equation:

$$(SE_k / k)^2 = (SE\ MCA_{H+CD} / MCA_{H+CD})^2 + (SE\ MCA_{HE} / Expected\ MCA_{HE})^2 \quad (4)$$

In this equation, SE_k is standard error of the k, SE MCA_{H+CD} and SE MCA_{HE} are standard err ors of observed and expected MCA respectively. A k value of less than one indicates a radioadaptive response. If k=1, it means that there is no radioadaptive (a simple additivity) effect. Finally, if k is significantly greater than 1, it means that a synergistic effect[1] was induced. The statistical significance of increased or decreased frequencies of chromosome aberrations was evaluated using Student's t-test.

3. Results

Table 1 shows the number of study participants, age, sex, and potential maximum annual dose from exposure to external gamma rays in 15 and 30 individuals from HLNRAs and NLNRAs respectively who participated in our study. Table 1 also shows the mean frequencies of chromosomal aberrations per cell with and without the 2 Gy challenge dose and whether there was a radioadaptive response. Overall results, show a statistically significant radioadaptive response with a k-value less than one (Table 2).

The age, sex, and mean cumulative effective radiation doses from exposure to external gamma rays in the 12 subjects are shown in Table 3. The average cumulative effective dose in the 7 residents of HLNRAs was 2500 mSv (2.5 Sv) which is about 170 times greater than for the 5 controls who received only 15 mSv. Table 3 also shows the mean frequencies of chromosomal aberrations per cell with and without the 1.5 Gy challenge dose and whether there was a

[1] Synergism means the observed effect of exposure to a combination of substances is greater than the sum of the effects of each substance administered individually (e.g. 2+2 = 5).

radioadaptive response. Five out of 7 residents of HLNRAs, demonstrate a statistically significant radioadaptive response with k-values less than one. The k-values were less than one but the differences were not statistically significant in 2 individuals with the highest cumulative effective doses (Table 4).

Table 5 shows no significant difference between background levels of MCA in non-irradiated cells of residents of HLNRAs and the controls. There were fewer chromosomal aberrations in the cells of the residents of HLNRAs exposed to 1.5 Gy compared to the controls ($P<0.001$).

After plotting the k-value versus cumulative lifetime dose, we fit a second-order polynomial curve to the data, forcing a y-intercept value of zero. This seems appropriate because, at zero dose, we do not expect to see induced chromosomal damage. The resulting curve is not unlike those suggested by other researchers reporting on adaptive response (Ikushima 1989a) and suggests that these results are consistent with adaptive response induced by exposure to the elevated levels of natural background radiation found in Ramsar as we reported earlier (Ghiassi-Nejad et al., 2002). What is important about these findings is the apparent relationship between the degree of adaptive response (indicated by the k-value) and cumulative lifetime dose among all study participants. The radioadaptive response of the residents of HLNRAs was more pronounced (lower k values) at higher cumulative doses except for 2 residents, whose cumulative doses were much higher than the others. That is, increased natural radiation decreased the *radiation* sensitivity of the cells. In view of the known detriment produced by exposure to high levels of radiation, this finding is expected and may reflect the transition from the adaptive response regime to the detrimental response regime in the radiation dose-response curve.

4. Discussion

Although the induction of adaptive response has been indicated in a wide variety of both in vitro and in vivo human studies, our study is the first extended experiment on the induction of adaptive response in humans by high levels of natural radiation. The overall results of the 1st phase of our study showed a significant adaptive response when the cultured lymphocytes of the 15 inhabitants of HLNRAs were exposed to a 2 Gy Gamma challenge dose. These results confirm the previous results obtained in other *in vivo* human studies such as radiation worker studies (Barquinero *et al.* 1995, Gourabi and Mozdarani *et al.* 1998).

The results obtained in the 2nd phase indicate that residents of areas with extraordinary levels of natural radiation (annual doses up to 260 mGy) show a significant radioadaptive response. It was observed that the 5 persons who received cumulative doses of 360-950 mGy showed a significant radioadaptive response while the two individuals with the highest cumulative doses (6800 and 8400 mGy) failed to show a significant radioadaptive response. That is, 70% showed an adaptive response from living in the HLNRAs. No participant from the HLNRA had an increase in radiation damage ($k>1$) compared to the controls.

We consider of great potential importance that high levels of natural radiation can serve as the priming or conditioning dose. Other human studies came from normal background areas and studies in which the adapting dose to the cells was given in vitro. These studies showed various responses as indicated in the following. There was a radioadaptive response in none of the three donors (Hain *et al.* 1992); in 2 of 6 donors (Pereira Luis and Pova 1992) and in 1 of 8

donors (Gajendiran 2001). In our study, the adaptive response observed in the residents who were exposed to doses up to 260 mGy y^{-1}, were significant.

In this study the k-values of the induced adaptive response ranged from 0.25 to 0.79 (Table 4). There was no significant difference between the $MCMA_{+0}$ of the residents of HLNRAs and NLNRAs (Table 5). This finding contradicts that of Fazeli (1990), who reported that numbers of chromosomal aberrations in lymphocytes of HLNRA residents were significantly higher than in NLNRA residents.

The following factors explain the importance of the radioadaptive response observed in the residents of VHLNRAs of Ramsar:

1. Studies on the inhabitants of the contaminated areas after Chernobyl accident showed no adaptive response in the lymphocytes of the inhabitants chronically exposed to fallout and then challenged with a high dose radiation (Padovani *et al.* 1995). However, when the same samples were challenged with bleomycin rather than ionizing radiation, an adaptive response was observed (Tedeschi *et al.* 1995). This may be due to living in an area with elevated levels of natural radioactivity for many years vs. living in a contaminated area for a much shorter time. Assessing the radioadaptive response of inhabitants who moved to the HLNRAs of Ramsar 5-20 years ago, is planned for the future.
2. Adaptive responses have been usually observed by exposing the cells *in vitro* to a low dose radiation in the range of 1-10 cGy (Redpath *et al*. 2001). These doses are considerably lower than the lifetime doses that induced adaptive response in the inhabitants of HLNRAs of Ramsar.
3. Excluding a few studies, which have been performed on the induction of radioadaptive response in radiation workers (Barquinero *et al.* 1995, Gourabi and Mozdarani *et al.* 1998), *in vivo* adaptive response studies were typically performed on laboratory animals. Extrapolating animal data to humans may not be valid.
4. The relative frequency of individuals who show no radioadaptive response in some *in vitro* studies (cultured cells were exposed to both adapting and challenge doses in a laboratory) is considerably greater than the frequency observed in this study (Hain *et al*. 1992, Pereira Luis and Povo 1992, Vijayalaxmi *et al*. 1995, Gajendiran *et al*. 2001).
5. Gadhia (1998) suggested that aging could abolish the adaptive response. He found statistically significant radioadaptive response in all of blood donors aged 5-45 years and no radioadaptive response in all 12 donors aged 65 years. We observed significant radioadaptive responses in 2 individuals who were much older than 65 years (Table 3). Our findings suggest that in *in vivo* studies, aging does not seem to influence the induction of radioadaptive response.
6. Our study suggests that high levels of natural radiation may enhance radiation-resistance in non-cycling lymphocytes. As the majority of our lymphocytes are in the resting phase phase(G_0), any implication of radioadaptive response in radiation protection strongly depends on the possibility of induction of radioadaptive response in G_0 phase. There is still a great controversy over the possibility of induction of radioadaptive response in G_0 of the cell cycle. While some investigators claimed the existence of a significant radioadaptive response in G_0 phase of the cell cycle, others reported that this response is only observable in cycling lymphocytes (Shadley *et al.* 1987, Moquet *et al.* 1989, Wang *et al.* 1991). Our results on the

high-level natural radiation induced radioadaptive response, clearly showed that the non-cycling lymphocytes of the inhabitants demonstrated a significant response.

7. We note that the seven data points assembled in this study appear to be a "U" shaped curve, similar in shape to those recently reported by Vilenchick and Knudson (2000) and other researchers (Ikushima 1989) in previous studies. Further work is needed to determine if this shape is maintained when more data are available.
8. Some of the discrepancies noted above may be due to the difference between administering the conditioning dose in vivo versus in vitro and over many years versus a short period of time. These discrepancies must be resolved through further studies in order to confirm the findings reported here and in our previous paper (Ghiassi-Nejad and Mortazavi 2001, Ghiassi-nejad et al., 2002). In particular, we feel that further studies in Ramsar are of sufficient importance that the international community, perhaps in conjunction with the RERF or the IAEA, should consider establishing a long-term research institute in Ramsar to help us gain a better understanding of the radiation biology and radioecology of this region.

Conclusion

Our studies suggest that chronic exposure to elevated levels of natural radiation could make the cultured lymphocytes more resistant to subsequent high doses of radiation. A relationship was found between the cumulative dose of each study participants and the magnitude of the induced radioadaptive response. Results of our experiments showed that high levels of natural radiation in inhabitants whose cumulative doses were up to 1 Gy significantly decreased radiation damage as measured by reduced chromosomal aberrations in irradiated lymphocytes. This can be considered a beneficial effect of high natural radiation. If the LNT hypothesis is true, public health is best served by relocating HLNRAs' inhabitants. However several statistically significant epidemiological studies of populations exposed to occupational doses of radiation show decreases of cancer mortality and mortality from all causes (Matanoski 1991, Pollycove 1998, and Berrington *et al.* 2001). Populations in areas with high levels of natural radiation such as Kerala, India (Nair *et al*., 1999; Jaikrishan *et al*., 1999) or Yangjiang, China (Tao *et al*., 2000) show no adverse health effects when compared to low-dose populations. Furthermore, several studies of large populations suggest beneficial health effects of higher than normal background doses of ionizing radiation, i.e., lower cancer mortality rates (Frigerio et al 1973; Cohen 1995, 1996; Wei 1997; Jagger 1998). Our findings on the biological effects of prolonged exposure to high levels of natural radiation in the inhabitants of VHLNRAs of Ramsar, showed no apparent harmful health effects. We have been reported previously that the health effects of prolonged exposure to high levels of natural radiation may contradict current ultra-conservative radiation protection regulations (Mortazavi et al. 2002c). Governments should adopt public health measures and policies that are cost-effective in risk reduction by considering the financial, social and psychological impact on their citizens (Karam et al., 2002, Mortazavi 2002). Based on our results we suggest that worldwide research on the residents of high level natural radiation areas help scientists better justify if LNT model of radiation risk is appropriate as the basis for public health measures.

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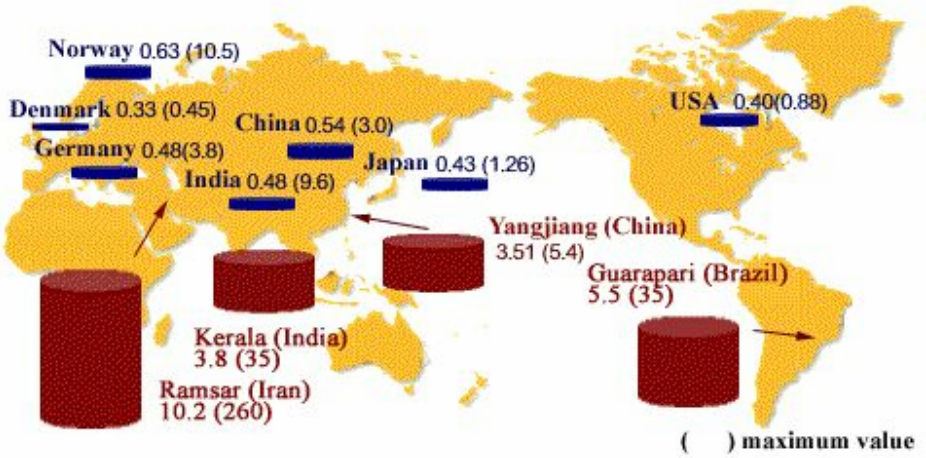

Figure 1. Average and Maximum annual background absorbed doses (mGy/yr) to the inhabitants of some countries and for areas with high levels of natural radiation (Used with permission of Radiation Research Foundation, Kyoto, Japan).

Table.1 Mean frequency of chromatid aberrations* in non-irradiated and 2 Gy irradiated cells of NLNRAs and HLNRAs residents.

Area	No. of Participants	Age (years)	Sex	Maximum Annual Dose (mGy)	MCA [c] in non-irradiated cells	MCA [c] in cells exposed to 2 Gy Gamma rays	Induction of radioadaptive response
HLNRAs [a]	15	30.40 ± 1.92	5F 10M	260	0.099 ± 0.003 [d]	0.111 ± 0.003	Positive (P<0.001)
NLNRAs [b]	30	33.77 ± 1.33	11F 19M	1.05	0.049 ± 0.003	0.167 ± 0.004	ND [e]

a Normal background radiation area
b High background radiation area
c Mean chromosome aberrations per cell
d Mean ± SE
e Not determined
** Gaps were included in the statistical analysis*

Table. 2 Induction of radioadaptive response in the residents of HLNRAs of Ramsar.

Cases	MCA[a]					k-Value
	Adapting Dose Alone	Challenge Dose Alone	Controls	**Expected**	**Observed**	
15 HLNRAs' Inhabitants [b]	0.099 ± 0.003 [c]	0.167 ± 0.004	0.049 ± 0.003	0.217 ± 0.006	0.111 ± 0.003	0.514 ± 0.055

a Mean chromosome aberrations per cell

b High background radiation area

c Mean ± SE

** Gaps were included in the statistical analysis*

Table.3 Mean frequency of chromatid aberrations in non-irradiated and 1.5 Gy irradiated cells of NLNRA and HLNRA residents.

Case No.	Age (years)	Sex	Cumulative dose (mSv)	MCA [c] in non-irradiated cells	MCA [c] in cells exposed to 1.5 Gy Gamma rays	Induction of radioadaptive response
1 (NLNRA) [a]	69	F	11	0.02 ± 0.01	0.17 ± 0.03	ND [d]
2 (NLNRA)	29	M	18	0.01 ± 0.01	0.14 ± 0.03	ND
3 (NLNRA)	37	M	12	0.02 ± 0.01	0.24 ± 0.04	ND
4 (NLNRA)	44	F	17	0.01 ± 0.01	0.16 ± 0.03	ND
5 (NLNRA)	26	M	15	0.02 ± 0.01	0.23 ± 0.04	ND
1 (HLNRA) [b]	23	M	360	0.01 ± 0.01	0.12 ± 0.02	Positive (P<0.05)
2 (HLNRA)	47	F	390	0.01 ± 0.01	0.13 ± 0.03	Positive (P<0.05)
3 (HLNRA)	70	F	360	0 ± 0	0.09 ± 0.03	Positive (P<0.01)
4 (HLNRA)	57	F	6800	0.02 ± 0.01	0.14 ± 0.04	Negative
5 (HLNRA)	63	M	8400	0.02 ± 0.01	0.15 ± 0.05	Negative
6 (HLNRA)	75	F	950	0.03 ± 0.02	0.05 ± 0.02	Positive (P<0.001)
7 (HLNRA)	55	F	480	0.01 ± 0.01	0.06 ± 0.02	Positive (P<0.01)

a Normal background radiation area
b High background radiation area
c Mean chromosome aberrations per cell
d Not determined
** Gaps were excluded in the statistical analysis*

Table.4 Induction of radioadaptive response in the residents of HLNRAs of Ramsar.

Case No.	MCA[b]					k-Value
	Adapting Dose	Challenge Dose	Controls	Expected	Observed	
1 (HLNRA) [a]	0.01 ± 0.01	0.19 ± 0.02	0.02 ± 0.004	0.18 ± 0.02	0.12 ± 0.02	0.67 ± 0.13
2 (HLNRA)	0.01 ± 0.01	0.19 ± 0.02	0.02 ± 0.004	0.18 ± 0.02	0.13 ± 0.03	0.72 ± 0.20
3 (HLNRA)	0 ± 0	0.19 ± 0.02	0.02 ± 0.004	0.17 ± 0.02	0.09 ± 0.03	0.53 ± 0.20
4 (HLNRA)	0.02 ± 0.01	0.19 ± 0.02	0.02 ± 0.004	0.19 ± 0.02	0.14 ± 0.03	0.74 ± 0.22
5 (HLNRA)	0.02 ± 0.01	0.19 ± 0.02	0.02 ± 0.004	0.19 ± 0.02	0.15 ± 0.03	0.79 ± 0.28
6 (HLNRA)	0.03 ± 0.02	0.19 ± 0.02	0.02 ± 0.004	0.20 ± 0.03	0.05 ± 0.02	0.25 ± 0.12
7 (HLNRA)	0.01 ± 0.01	0.19 ± 0.02	0.02 ± 0.004	0.18 ± 0.02	0.06 ± 0.02	0.33 ± 0.13

a High background radiation area
b Mean chromosome aberrations per cell
** Gaps were excluded in the statistical analysis*

Table.5 Frequency of chromosomal aberrations in non-irradiated and irradiated cells of the residents of high background radiation areas and the residents of the control area.

Study group	Sample size	Cumulative dose (mSv)	MCA[a] in non-irradiated cells	MCA[a] in cells exposed to 1.5 Gy
HLNRA[b]	7	2534	0.014 ± 0.004	0.106 ± 0.015
NLNRA[c]	5	14.6	0.016 ± 0.002	0.188 ± 0.020
P-value[d]			Not significant	< 0.001

a Mean chromosome aberrations per cell
b High background radiation area
c Normal background radiation area
d Student's t-test.
** Gaps were excluded in the statistical analysis*