Applicability of Translocations in Chromosomes of Lymphocytes for Retrospective Assessment of Absorbed Doses (FISH-Method)

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It is generally accepted that the analysis of instable chromosome aberrations (dicentrics and centric rings) permits the reconstruction of absorbed doses immediately after radiation exposure or if little time has passed since the exposure occurred [4]. In case years have passed after the exposure, dose assessment by means of analysis of the level of unstable chromosome aberrations is possible only using a correction factor characterizing the rate of decline of dicentrics and centric rings with time. Analysis of the dynamics of temporal decline in the level of cells with unstable chromosome aberrations was the subject of several studies [1,2,3,5,9]. Linear, exponential or other relationships have been obtained permitting the determination of the half-life of dicentrics and centric rings in peripheral blood.

According to the data obtained by us in the course of a 7-year follow-up of the liquidators participating in rescue and clean-up operations in Chernobyl, this period is about four years. However, we have no possibility to determine the coefficient of reduction of the level of unstable chromosome aberrations in individuals exposed to radiation 40 years ago by means of direct analysis of the dynamics of this process. The only possibility for making such calculations which are so important for biological dosimetry is the comparison of the rates of stable and unstable chromosome aberrations. It is known that in the early period after exposure the ratio of stable and unstable chromosome aberrations makes up 1:1 if the FISH-method is used [7,10,11,13] and if there is a possibility to identify dicentrics using pancentromeric probes [8]. It is apparent that this ratio will be changing with time in favor of stable aberrations.

Hence, using the ratio of stable and unstable chromosomes it is possible to study the dynamics of unstable chromosome aberrations in time. This requires that such ratios should be experimentally determined at different periods after the action of ionizing radiations. In the previous publications [12-14] we have presented the rates of stable and unstable chromosome aberrations estimated in the liquidators within 8-9 years after the Chernobyl accident, in the population of the Three Mile Island (USA) region within 15 years after the nuclear reactor accident in 1979 and in the populations of several localities of the Altai Territory within 45 years after the nuclear tests in 1949. These materials can be used for analysis of the dynamics of the rate of cells with dicentrics and centric rings.

Fig. 1 presents the results of such analysis. The left scale demonstrates the decline of the level of cells with dicentrics and centric rings in the liquidators (triangle points). The initial number of such cells observed immediately after the exposure in 1986 is taken as 1. The right scale gives the ratio of cells with dicentrics and centric rings to the number of cells with translocations recorded by the FISH-method. The ratio of such types of chromosome aberrations immediately after the action of ionizing radiations makes up 1:1 [8]. The left and right scales are completely identical and thus make it

possible to examine in relative values the dynamics of unstable chromosome aberrations over a long period of time. All calculations are given with corrections for control levels.

It is seen that the experimental points characterizing the relative portions of dicentrics and centric rings at different periods of the follow-up of different groups demonstrate a regular decrease in the level of these aberrations over several decades. The results obtained make it possible to calculate as a first approximation correction factors that can be applied for reconstruction of absorbed doses on the basis of analysis of the observed level of cells with dicentrics and centric rings.

The period in which the number of cells with dicentrics and centric rings is reduced to 0.5 is about 4 years in the given case. After 10 years about 25% of the initial number of such cells (correction factor 4) remain in the peripheral blood. For three localities of the Altai Territory the correction factor was derived to be about 7 for a time delay of 45 years since the exposure to ionizing radiations. It is interesting to note that we found a ratio of about 14 in the control material for the cells with translocations compared to the cells with dicentrics and centric rings.

It should be noted that the reconstruction of doses with the use of this approach is possible only in situations where comparatively high doses have been absorbed, due to which a statistically significant excess of the level of cells with dicentrics and centric rings over the control level is observed in the examined group.

References:

1 Bauchinger, M., Schmid, E., Braselmann, H., Willich, N., Clemm, C.: Time-effect relationship of chromosome aberrations in peripheral lymphocytes after radiation therapy for seminoma. Mutat. Res. 211 (1989) 265-272

2 Brewen, J.G., Preston, R.J., Littlefield, L.G.: Radiation-induced human chromosome aberration yields following an accidental whole-body exposure to Co-60 gamma rays. Radiat. Res. 49 (1972) 647-656

3 Buckton, K.E., Smith, G.G., Court Brown, W.M., in Radiation Cytogenetics, North Holland, Amsterdam 1967, p. 106-114

4 Int. Atomic Energy Agency: Biological dosimetry: chromosomal aberration analysis for dose assessment. IAEA Techn. Rep. 120, Vienna 1986

5 Lloyd, D.C., Purrot, R.J., Reeder, E.J.: The incidence of unstable chromosome aberrations in peripheral blood lymphocytes from unirradiated and occupationally exposed people. Mutat. Res. 72 (1980) 523-532

6 Lucas, J.N., Tenjin, T., Straume, T., Pinkel, D., Moore II, D., Litt, M., Gray, J.W.: Rapid determination of human chromosome translocation frequency using a pair of chromosome-specific DNA probes. Int. J. Radiat. Biol. 56 (1989) 35-44

7 Lucas, J.N., Awa, A., Straume, T., Poggensee, M., Kodama, Y., Nakano, M., Ohtaki, K., Weiser, H.-U., Pinkel, D., Gray, J., Littlefield, G.: Rapid translocation frequency analysis in human decades after exposure to ionizing radiation. Int. J. Radiat. Biol. 62 (1992) 53-63

8 Nakano, M., Nakashima, E., Pawel, D.J.: Kodama, Y., Awa, A.: Frequency of reciprocal translocations and dicentrics induced in human blood lymphocytes by X-irradiation and determined by fluorescence in situ hybridisation. Int. J. Radiat. Biol. 64 (1993) 565-569

9 Preston, R.J., Brewen, J.G., Grengozian, N.: Persistance of radiation-induced chromosome aberrations in marmoset and man. Radiat. Res. 60 (1974) 516-524

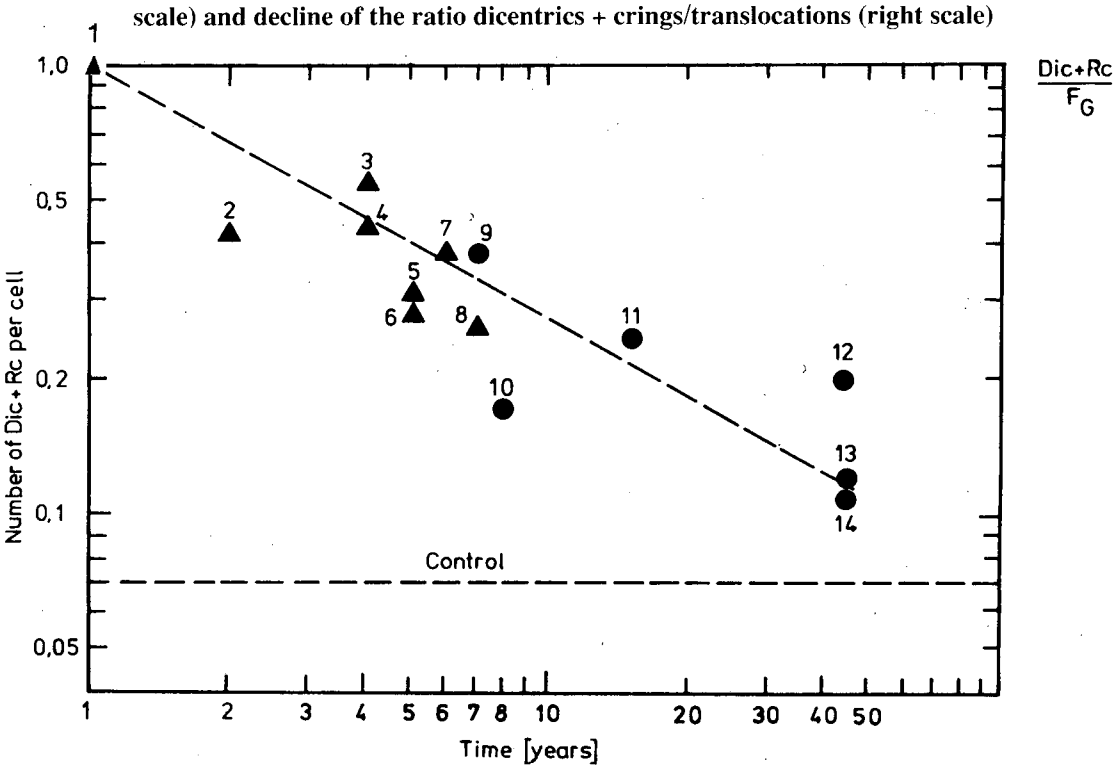
10 Ramalho, A.T., Nascimento, A.C.H., Natajaran, A.T.: Dose assessments by cytogenetic analysis in the Goiania (Brazil) radiation accident. Rad. Prot. Dos. 25 (1988) 97-100

11 Salassidis, K., Schmid, E., Peter, R.U., Braselmann, H., Bauchinger, M.: Dicentric and translocation analysis for retrospective dose estimation in humans exposed to ionizing radiation during the Chernobyl nuclear power plant accident. Mutat. Res. 311 (1994) 39-48

12 Shevchenko, V.A., Snigiryova, G.P.: Cytogenetic effects of the action of ionizing radia-

tions on human populations. In E.B. Burlakova (Ed.), Consequences of the Chernobyl catastrophe. Center for Russian Environmental Policy, Moscow 1996, p. 23-45
13 Shevchenko, V.A., Snirgiryova, G.P.: The possibility of the reconstruction of the absorbed doses by FISH-method among the populations of the Altai Region exposed by nuclear testing. Bulletin Research Programme "Semipalatinsk Test Site/Altai 1 (9) 1996, 40-49
14 Snirgiryova, G.P., Shevchenko, V.A., Novitskaya, N.N.: Using FISH for retrospective dose estimation in persons who took part in liquidation of the Chernobyl accident consequences. Rad. Biol.Rad. Ecol. 35 N5 (1995) 654-661 (in Russ.)

Figure 1:
Decline of dicentrics and centric rings in human lymphocytes after exposure (left scale) and decline of the ratio dicentrics + crings/translocations (right scale)



points 1-8 (triangles) and left scale:
number of dicentrics and centric rings per cell in lymphocytes of liquidators measured at different times between 1987-1993 (relative units)

points 9-14 (circles) and right scale:
ratio of cells with dicentrics and crings to cells with translocations measured in different exposed populations

9 Klimovo, Bryansk region
10 liquidators of the Chernobyl accident
11 TMI region (USA)
12-14 several localities of the Altai Territory affected by nuclear tests in Semipalatinsk