FISH Translocation Practice as a Retrospective Biodosimeter: a Review.

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Purpose : The purpose of this study, based on the 64 analysed cases, is to check whether this indicator of dose is appropriate and to identify its remaining limits.

Material and methods : Translocations were detected on lymphocytes of patients who have been suspected of overexposure to ionising radiation in the past. Chromosomes 2, 4 and 12 were labelled using the 3 painting FISH technique.

Results : Among the 64 cases, 35 cases presented a positive dose with translocations. The lowest positive dose measured was 0.3 Gy. Between 2 and 6 months, the dose measured by translocations is higher than that measured by dicentrics so translocations estimated a dose accumulation. Over 6 months, dose estimation is only possible by translocations because dicentric dose estimation is close to 0. We were able to measure an over exposition up to 30 years.

Conclusion : This technique is helpful to identify exposed people. However the detection limit of the technique is still higher than the conventional cytogenetic technique based on the scoring of dicentrics. In addition, no clear relation can be established between exposition and late pathologies developed by the patients.

Keywords: FISH; Translocations; Retrospective Dosimetry; Lymphocytes; Accidental overexposure; Ionising Radiation

1. INTRODUCTION

Radiation accidents can arise from nuclear reactors, industrial or medical sources, as well as in research centres where radioactive material is used. After an accident, dose reconstruction can be done by the evaluation of clinical symptoms, and by physical or biological dosimetry. Biological dosimetry can improve the diagnosis by evaluating the radiation induced variations of some biological parameters.

Among the different endpoints used in biological dosimetry for dose assessment, evaluate the yield of dicentrics induced by radiation in lymphocytes is the reference method (Edwards 1997; Voisin, Benderitter et al. 2001). However this type of aberrations is unstable through the time and it do not allow estimating the dose received long time before the analysis. Translocations, another type of chromosome aberrations, are more stable through the time and can be used for retrospective studies. A consensus arises and simple complete translocations observed in stable cells are considered as the aberrations of choice for retrospective dosimetry (Bauchinger, Schmid et al. 1993; Barquinero, Cigarran et al. 1999; Edwards, Maznik et al. 2002; Gregoire, Sorokine-Durm et al. 2006). Translocations can be easily detected by using the Fluorescent In Situ Hybridisation (FISH) technique.

Here it is presented an historical report of the analysis on retrospective biological dosimetry carried out at the IRSN during the last fifteen years.

2. RESULTS AND DISCUSSION

It was chosen to use the FISH technique in complement to the conventional cytogenetic technique based on the scoring of dicentrics when the delay between exposure and analysis exceeds 2 months. To identify the potential overexposure of those patients, their level of translocations is compared to the background level of translocations in the French population established in the laboratory. Considering the fact that the delay

between exposure and expertise is up 2 months, we applied the FISH technique in order to compare the dose estimated by translocations and the one estimated by dicentrics.

64 overexposure suspicions were analysed by retrospective dosimetry at IRSN since 1995. Among these 64 cases 35 presented a positive translocation rate significantly different of the background level. The different cases have been classified in several groups; militaries, public, hospitals, industries using radioactivity and electronuclear. The majority of expertise requirements come from the military group. In this group the number of positive cases reached 70% of cases analysed. The second important group in terms of number of total cases analysed was the public people who was not supposed to be in contact with ionising radiation. Surprisingly, the number of positive cases represented 68% of all cases analysed at IRSN. The three other groups were workers from private hospitals, industries using radioactivity and the electronuclear group. On average the positive cases represented only 33% of analysed cases of these categories.

Positive cases can also be divided in two categories. The First one presented a delay between exposure and dose assessment from six months to several years. Due to this delay it is not surprising to observe a significant difference between the translocation dose and a dicentric dose close to zero. When dose estimations obtained by translocations were higher than those obtained by dicentrics this could reflect the measurement of the disappearance of dicentrics. The Second one presented a delay between exposure and analysis below six months. In these cases estimated doses by translocation and dicentric are then closer. When the translocation dose and dicentric dose could be compared, it has been showed that the minimum dose detected by FISH technique was 0.3 Gy which is in accordance to the described limit of the FISH technique (Edwards, Voisin et al. 2004). It highlights a main limitation of this technique for retrospective biological dosimetry purpose.

The FISH doses are given as an indication and in order to compare with the estimation dose from dicentric. However the dose estimation by FISH technique has no sense when the delay between exposure and analysis is over than 10 years.

Conclusion

The main interest of translocations is their stability compared to dicentrics. So, this technique allows an estimation of a dose a long time after an ionising radiation exposure supposed or real whereas dicentrics have disappeared. Since the application of the FISH technique to retrospective overexposure assessment, the number of cases increases regularly. However the sensitivity of this technique is lower than the conventional cytogenetic technique is. Indeed even if the laboratory has a low background level the minimum detectable dose remains 0.3 Gy. As the public is the main exposed category, a good knowledge of harmful of radiation should limit the number of accident. Actual researches are going to find a bio indicator of irradiation with the stability of translocations and the specificity of dicentrics.

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