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Dose Fractionation Concept in Radiation Protection to Standardize Risk/Dose Limits and Epidemiology Studies

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Ionizing radiation, either originated from natural background (NBG) radiation sources (primordial radioactive materials in the earth crust and cosmic rays) or from man-made sources (reactors, accelerators, diagnostic and radiotherapy equipment, industrial sources, etc.) expose the public and workers (as members of public) which may cause chemical and biological changes in the human body cells and may damage them temporarily or permanently [1]. Some cells may die (apoptosis), some become abnormal either temporarily or permanently, or some have damages in the DNA as a genetic material which may cause cancer. The cell may also make self-repair depending on the severity of the damage and continue survival like a normal cell. The extent of the damage to the cells depends on many radiation exposure factors such as the radiation type and its energy, LET, dose and dose rate, type of cell at risk and its sensitivity, cell oxygenation, environmental conditions, and whether or not the dose delivered to the cells is continuous or "fractionated" over time, a concept which has not been considered in the field of "radiation protection" so far.

Over the past few decades, major efforts have been in progress worldwide on applying low dose/low dose rate ionizing radiation exposures to epidemiological studies of public and in particular radiation workers to estimate radiation health risks per unit dose to either further support the "linear no-threshold (LNT) model" being presently practiced or the "hormesis model" or any other acceptable models [2-5]. In fact, this is one of the main challenging issues in the present radiation protection philosophy of the workers, public, and environment in ionizing radiation applications to have scientifically acceptable radiation health risks per unit dose of ionizing radiation to set standardized "dose limits" [6]. Presently, the dose limitation system and epidemiology studies of workers are based on considering only the highly "fractionated" occupational exposure with no consideration of any other doses received from sources such as chronic "unfractionated" NBG radiation in daily living indoors and outdoors, from which public and workers (as members of the public) are continuously exposed to [1,7-9]. In this context, it is the purpose of this "Editorial" to highlight and emphasize three important concepts in order to have "conservation of cause and effect" in radiation protection [7-9]; (i) integrate occupational doses with other radiation doses a worker receives also as a member of public, (ii) emphasize further the role of doses other than occupational exposure such as the NBG radiation in estimation of radiation risks and setting dose limits, and in particular (iii) introduce and demonstrate the role of "fractionation" of doses received by radiation workers in the calculation of the integrated doses; concepts which have not yet been of concern in the present radiation protection system [6].

As a known principle in experimental radiobiology, as the radiation dose delivered to cells increases, the number of cells survived or the survival fraction decreases. The shape of the survival curves depends on the radiation type and energy, LET, dose and dose rate (dose per unit time), state of fractionation of doses, oxygenation, temperature, etc. In fact, for the cell killing, a prescribed dose is required to be delivered with a known dose rate within a certain period of time. When the same prescribed dose is divided into several fractions, the total dose given in order to observe the same effects, for example for cell killings, should be increased. This is due to the self-repair mechanisms that occur in a damaged cell within few hours post irradiation depending on the factors as discussed above.

In radiation therapy, dividing a prescribed radiation dose to a tumor to kill the cancerous cells into multiple smaller dose fractions is commonly referred to as "dose fractionation" [10]. The "dose fractionation" is applied in order to maximize the positive effects of radiation by destroying the cancerous cells to be killed and to protect the normal cells by minimizing any negative effects. In fact, at the cellular level and at doses concerned in radiation therapy, five important biologic processes occur after each radiation treatment, which produces the benefit of fractionated dose in radiation therapy. These biological processes include repair of the sublethal DNA damage by normal cells; repopulation of normal healthy cells, reassortment of tumor cells into more radiosensitive phases of the cell cycle; reoxygenation of tumor cells and radiosensitivity [10]. While such processes have been relatively well studied at high doses and dose rates used in radiation therapy, it seems data on such effects occurring at very low doses and dose rates (e.g. 10 μSv.h^{-1}) encountered in radiation protection need to be developed. At such low doses and dose rates in particular for low-LET radiation such as gamma rays, the interactions of radiation with the DNA molecule in a cell are expected to cause single-strand breaks which are more susceptible to be repaired as can be well noted on the shoulder of the gamma survival curves. While in radiation therapy at high doses, double-strand DNA breaks are expected to be common making the cells more probable to be killed rather than repaired. Therefore, self-repair of cells at very low doses and dose rates common in radiation protection can effectively occur, as is observed on the shoulder of the survival curves.

While the level of doses and dose rates has been highly important in observing radiobiological effects, the "fractionation of doses" at such levels has not yet been noted in order to equalize and standardize radiation effects and risks per unit dose for setting dose limits and in particular for epidemiology studies of workers. However, it should be noted that the

doses of an individual member of public from environmental radiation in particular from NBG radiation are usually chronic and "unfractionated", while those of the occupational exposure of workers are unavoidably highly "fractionated" for which relevant corrections should be applied. This "dose fractionation concept" has been recently introduced in radiation protection by a new "Universal Radiation Protection System (URPS) Hypothesis" proposed by this author [1,7-9]. The "URPS Hypothesis", based on 3 main principles, given below [1]:

1. Assigns equal radiation health risks to an individual (either a member of public or a worker also as a member of public) per unit radiation dose either from NBG radiation or from man-made sources,

2. Applies a "Standardized Integrated Dose System" (SIDS) to any dose limits, reference levels, etc. based on integrating all doses an individual receives from the existing exposure (e.g. NBG radiation), planned exposure, and emergency exposure situations in order to standardize the integral doses an individual, in particular, a worker receives for setting dose limits and for estimating health risk in epidemiological studies, and

3. Takes into account any factors affecting the effects of an individual dose, in particular, the dose "fractionation factor" in setting integral health risk-based dose limits and reference levels in radiation protection in general and in any epidemiological studies of an individual such as that of workers in particular.

An individual, a member of "public" or a "worker", receives radiation effective doses (mSv.y^{-1}), used also as dose in this Editorial, mainly from three types of exposure situations such as [6];

- Planned exposures, for example in countries with nuclear power industry, within an ICMP dose limit of 1 mSv.y^{-1} (dose limit of public),

- Existing exposures usually from environmental radiation such as the NBG radiation (or from the past practices) which are usually chronic and "unfractionated" exposures. The UNSCEAR global mean value of 2.4 mSv.y^{-1} is the mean value of the mean national NBG exposures; an exposure different from one country to another [11],

- Emergency exposure situations such as in Chernobyl or Fukushima nuclear power plant accidents with a situation depending on the location, time, etc.

A "worker" receives radiation exposures as an individual member of the public, and in addition as a "worker" from occupational exposure in daily work. While the doses of a "worker" received as an individual member of the public for example from NBG radiation are "unfractionated", doses received occupationally by a worker is highly "fractionated". The doses received by a member of public other than NBG radiation such as medical exposure which contributes to a major part of mean national public exposure is highly "fractionated" and for the purpose of the demonstration below it has not been considered here.

According to the "URPS Hypothesis" [1], the "fractionated" occupational doses and chronic "unfractionated" doses as an individual member of the public from existing and planned exposure situations being usually "unfractionated" should be considered in estimating the integrated effective doses of a worker. The "dose fractionation" has, in fact, a serious effect on radiation protection philosophy, concepts, and procedures and in turn on the integral annual effective dose of a worker. By considering the dose of an exposure situation and its relevant fractionation factor, the effective dose of a "worker" can be formulated in equation (1), as follow:

$$^{w}I_{aid}(mSv.y^{-1}) = E_{o}xF_{o} + E_{nbg}xF_{nbg} + E_{pes}xF_{pes} + E_{po}xF_{po} \qquad (1)$$

Where;

$^{w}I_{aid}$= Annual integrated dose of a worker (mSv.y^{-1}),

E_{o}=Annual occupational dose (mSv.y^{-1}),

F_{o} = Fractionation factor for occupational dose,

E_{nbg}=Annual national mean NBG dose (mSv.y^{-1}),

F_{nbg}=Fractionation factor for NBG dose,

E_{pes}=Annual dose from planned exposure situation as a member of public (mSv.y^{-1}),

F_{pes}=Fractionation factor for planned exposure situation effective dose,

E_{po}=Annual public other dose, and

F_{po}=Fractionation factor of other doses.

Therefore, the annual integrated dose of a worker $^{w}I_{aid}$ (mSv.y^{-1}) can be given as a general equation (2):

$$^{w}I_{aid}= \Sigma_{i}E_{i}. F_{i} \qquad (2)$$

Where;

$^{w}I_{aid}$= Worker's annual integrated dose (mSv.y^{-1}),

E_{i}=Effective dose of exposure type (i)(mSv.y^{-1}), and

F_{i}= Fractionation factor of exposure type (i).

The reason why the occupational exposure is considered highly fractionated has been discussed before [1,7-9]. However, for the purpose of this editorial, a para from a previous article is quoted here [8]: "A worker for example in France, in the United Kingdom (UK) and in the United States of America (USA) or in many other countries in the world works 250 days in 50 weeks per year and 8 hours per day making a total of 2000 man-hour work per year. There are at least 16 hours between two occupational exposure periods during week days and about 68 hours during the weekends, at least 15 days during annual leaves in developed countries and very long durations in some developing countries due to many holidays" [8]. As discussed above, since the occupational exposure is highly fractionated, a "fractionation factor" should be applied to occupational doses for estimating health-related risks of radiation workers as well as for setting dose limits. The "fractionation factor" can be applied to any radiation exposure depending on the degree of its continuity and fractionation no matter it is for a worker or for a member of the public.

Of course considering no fractionation effect in the integration of doses for example for occupational exposure or epidemiology studies is highly conservative and protective, but the URPS concept shows that this can be too protective for which a high cost should be paid. On the other hand, by considering a "standardized approach" by applying fractionation factors in the integrated dose calculations for real consideration of cause-effect and for cost-benefit analysis, the "monetary value of the man-Sievert" and accordingly the cost of nuclear installations, for example, nuclear power will be much reduced, radiophobia will be much reduced, and among other things, it constructs a bridge between the LNT model and the hormesis model. Conservatism in radiation protection has been always a principle but too much conservatism is highly costly and cannot be justified.

In order to demonstrate the "dose fractionation concept" in radiation protection graphically, an example of an individual USA radiation worker (due to the availability of the relevant exposure data) is applied. Also for this demonstration, only major doses such as from the NBG radiation and occupational exposures have been considered. This individual is a participant of the international nuclear worker's study (INWORKS) (France, the UK, and the USA) who has received for example a mean

cumulative dose of 25 mSv from an occupational exposure with a mean attained of 58 y age [4,5]. The worker, also as a member of public, has additionally received 6.2 mSv.y^{-1} mean national public exposure; 3.1 mSv.y^{-1} from chronic NBG radiation and 3.1 from other sources from which medical exposure is the major part [12], but only NBG radiation dose is considered in this demonstration. Accordingly, this worker has received from birth approximately 58 y × 3.1 mSv.y^{-1}=180 mSv from the "unfractionated" NBG doses with an assumed fractionation factor (F_{nbg}) of approximately1.0 and lifetime occupational dose of 25 mSv applying a variable occupational fractionation factor (F_o) of 0.1 to 1.0. By applying the equation (2) using the relevant dose and F values, Figure 1 was generated demonstrating the worker's integrated lifetime dose as a function of the F_o once considering only the mean cumulative "fractionated" occupational dose of 25 mSv (lower response) and once by integrating these values with a mean attained of 58y age lifetime "unfractionated" NBG radiation dose (180 mSv) (upper response).

As can be seen in Figure 1, as F_o decreases, i.e., the time between fractionated dose increases, the effective occupational dose decreases; an actual situation in occupational exposure. On the other, when the occupational dose is modified by the varying F_o and added to the 180 mSv NBG dose, it can be seen that the NBG dose dominates and in fact the occupational dose has a very limited role even if F_o=1 is applied. Figure 1 highly demonstrates the role of the NBG radiation in the integrated dose and the role of F_o in the reduction of the actual occupational dose a worker has received, what has not been considered so far in radiation protection practices worldwide. By the time an exact value for F is determined, a fractionation factor of F_o=0.5 will highly improve the real effects of occupational exposure. In fact, if we assume that the available ICRP risk factors are the best based on the present state-of-the-art understanding of health risk estimates, then the present dose limit for occupational exposure by considering a medium value of F_O=0.5 can be doubled, as an example.

The exact F_o has yet to be carefully determined and standardized for global use. However, variations in F_o, as shown in Figure 1, demonstrate that if the occupational dose is fractionated, its value is rather very low compared to that of the NBG dose. If other doses are also integrated, then the occupational dose as it is now would be even ignorable within the fluctuations of other exposures. In particular, this "dose fractionation concept" is extremely important to be applied in epidemiology studies in general and for occupational exposure in particular since presently, only occupation exposure or even mostly external exposures have been considered in epidemiology studies of workers [2-5].

In conclusion, the author believes that the philosophy, concept and procedures proposed under the "URPS Hypothesis" are novel scientific and practical disciplines with a vision, strategy, and program for global standardization of radiation protection [1,7-9]. In particular, the introduction of "dose fractionation concept" in radiation protection through "integration of doses" can evolve the present understanding and status of the implementation of radiation protection worldwide. The health risk factors being presently used in radiation protection practice applying the LNT concept based on the Hiroshima and Nagasaki exposure situation, which is itself relatively "unfractionated" exposure applied to occupational "fractionated" exposures, and epidemiological health risk studies of radiation/nuclear workers presently in progress based on only occupational exposure or even only external exposure [2-5], may be compromised. The author humbly invites specialists in radiation protection to provide their outstanding feedbacks to the concepts proposed under the "URPS Hypothesis" in order to further validate the concept, if needed, towards establishing a "Universal Radiation Protection System" with a "Standardized Integrated Dose System" worldwide as radiation protection system of the 21st century.

Acknowledgement

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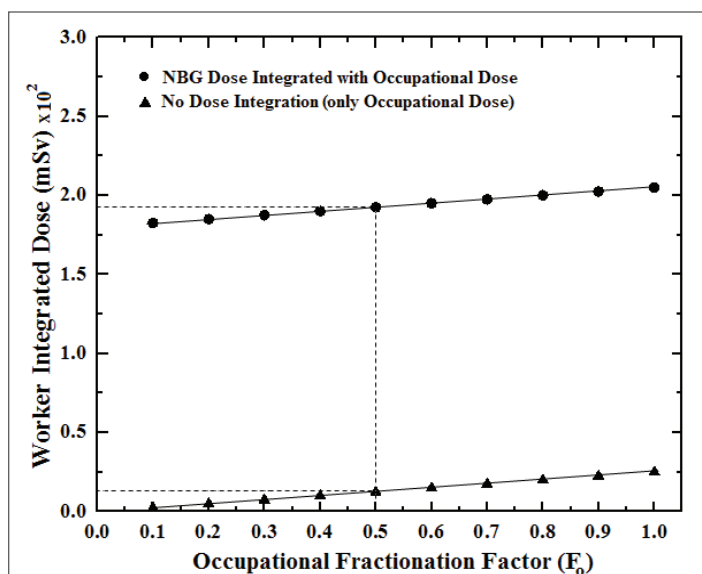
Figure 1: A worker integrated lifetime dose as a function of the occupational fractionation factor (F_o); once considering only the mean cumulative "fractionated" occupational dose of 25 mSv (lower response) and once by integrating these values with a mean attained of 58 y age lifetime "unfractionated" NBG radiation dose (180 mSv) (upper response).

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