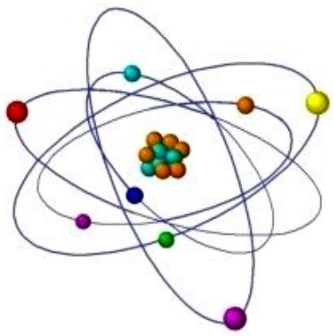
CAN CHRONIC RADIATION BE RADIOPROTECTIVE FOR PLANT SUBJECTS EXPOSED TO THE INHIBITING ACTION OF ACUTE GAMMA RADIATION?

(low-dose radiotherapy, "reverse radioadaptation")



[1]Oleksandr Mikhyeyev*, [2]Oksana Lapan
[1]Institute of Cell Biology and Genetic Engineering, National Academy of Science of Ukraine
[2]National Aviation University, Ukraine

https://doi.org/10.63465/rrs520258986 *Corresponding author: Email: mikhalex7@yahoo.com

ABSTRACT: *A new classification of types of radio-modifying effects is proposed, both in terms of the sequence of action of the main (inhibitory and hormesis doses) and modifying factors and in terms of the sign (direction) of the radio-modifying influence. The division of adaptive reactions into ordinary, hypo-, and hyper adaptive reactions is substantiated. Special attention in the work is given to the effects of positive post-radiation modification, essentially having, in the case of using ionizing radiation, the nature of radiotherapy (non-oncological), that can be conditionally called 'reverse radio adaptation'. Experimental evidence of its existence is presented, which can be the basis for the method of 'low-dose radiotherapy' of radiation damage.*

Key words: radiation hormesis, modification of radiation, hyper radio adaptation, reverse adaptation

INTRODUCTION

The scientific metric analysis of publications in radiobiology and radioecology shows that about a third of these works are dedicated to studying pre- and post-radiation modification of radiobiological effects. This focus makes sense as the ultimate aim of radiobiology and radioecology, predominantly serving human interests, is to develop a unique "set of tools" or levers for managing radiobiological reactions to minimize or maximize their consequences. If radiation modification is understood as the processes and results of influencing the outcome of radiobiological reactions, and limited to considering only the inhibitory effects of acute ionizing radiation exposure, then a general classification of radio-modifying factors (methods, influences, etc.) can be proposed, which can be any agent in nature – from physical to biological (see Tables 1 and 2). As seen from the content of the tables we do not use the concept of 'radioprotection' widely applied when describing radio modifying effects (Grodzinsky, Gudkov, 1973; Rozhdestvensky, 1985) due to its overly broad (ambiguous) content. On the other hand, we allow a broader interpretation of 'radiotherapy' understanding it not only as a the method of treating oncological diseases but also as the result of positive use of ionizing radiation in the post-radiation period, i.e., after the object receives the 'main' (inhibitory) dose, the radiotherapeutic (according to our classification) action of a factor of any nature in the corresponding dose/power/concentration/activity, etc.

Table 1. Classification of the types of radio modifying effects in terms of the sequence of action of the main radiation (testing in inhibitory dose/power/concentration, etc.) and the modifying factor of any nature.

Radio modification			
Preradiation		Postradiation	
Positive (radio prophylaxis, ‘radio adaptation’, ‘adaptive response’, hyper-radio adaptation)	Negative (preradiation sensitization, hyporadio adaptation)	Positive (non-oncological radiotherapy, reverse radio adaptation')	Negative (postradiation radiosensitization)

Table 2. Classification of the types of radio-modifying effects of factors of any nature based on the sign (direction) of the radio-modifying influence during the inhibitory action of ionizing radiation.

Radio modification			
Positive		Negative	
Preradiation (radio prophylaxis, ‘radio adaptation’, ‘radioadaptive response’, hyper-radio adaptation)	Postradiation (non-oncological radiotherapy, ‘reverse radio adaptation’)	Preradiation (preradiation radiosensitization, hyporadio adaptation)	Postradiation (postradiation radiosensitization)

Why do we put ‘radio adaptation’ and ‘radio adaptive response’ in quotes? Traditionally, ‘radio adaptation’/’radio adaptive response’ refers to a new state of a biological object in which it demonstrates increased radio resistance compared to the original to the action of a radiation stressor. However, it is clear that any biological object, if it can maintain its qualitative specificity and/or individuality, is thus already accommodated (adapted) to a complex of external and internal factors. In other words, a biological object in a state of adaptability (adaptedness) maintains the values of its structural-functional indicators (parameters, properties) at the previous (original, constitutive, endogenous, background, control) level. This state can be called ‘ordinary adaptation’ or ‘ordinary adaptedness’. It is also clear that the original state of the object can be changed under the influence of any exogenous or endogenous factor, and it, ultimately, or at some stage of the post-factor period will have either an unchanged level of resistance (‘ordinary adaptedness’) or changed. Thus, after the impact of any modifying factor at a specific point in time, the object can be in one of the following states:

original adaptation (adaptedness, adaptability) in terms of resistance (the biological object has a constitutive, ‘ordinary’ current, ‘control’ level of adaptedness); original adaptedness (like all other types of adaptedness) can also be cross, i.e., manifest in relation to other factors;

hyper adaptation (super adaptability) in terms of resistance (corresponds to the state of eustress according to H. Selye (1982)), in which the original resistance of the object to subsequent effects of the same or different (cross hyper adaptation in terms of resistance) factor is increased to some extent;

hypo adaptation (decreased resistance, ‘under adaptability’) in terms of resistance (the state of distress according to H. Selye (1982)), associated with a decrease in its original (current) resistance (similarly - cross hypo adaptation in terms of resistance). In this regard, depending on the type of acting factor and the type of ‘acquired’ adaptability, it is necessary, for example, to talk about hyper-radio adaptability, hypothermia adaptability, etc.

In the biological literature devoted to the problem of adaptation, practically no attention is paid to the fact that changing the degree of adaptability of an object is incorrectly described using only the concept of ‘adaptedness’, since, as we have already said, the object is always in a state of adaptedness of a certain level. We, talking about hyper- or hypo adaptedness, emphasize the need to characterize the direction of change of the original level of adaptedness with the corresponding terms.

It is especially important to emphasize this issue when considering radiobiological phenomena, which allows avoiding the ambiguity of the often used concept of ‘radioadaptive response’, which inadequately reflects the observed phenomenon (increase in the level of original radio adaptability) since, in fact, any reaction of an object to the impact is adaptive. Another matter is in which direction (decrease or increase) the level of original adaptability of the object will change.

As for the modification of positive (hormetic, hyperbiotic, etc.) effects of ionizing radiation (Kuzin, 1995), attempts to classify its possible types, as far as we know, were not made. As a working version of the classification of radio hormesis effects, the following is proposed (see Tables 3 and 4).

Tables 3 and 4 classify the types of modification of the radio hormesis effect of ionizing radiation by factors of any nature. It is noted that this classification is somewhat cumbersome in terminological terms, as it does not use established terminology, which simply does not exist. This is not surprising, since the phenomenon of radiation hormesis and the based-on-it phenomenon of hyper-radio adaptation (Mikheev, 2015) have not yet gained ‘recognition in the wider radiobiological community’. It is also clear that the time has not come yet for the realization of the need to study the modification of such an ‘elusive’ effect as radiation hormesis.

Table 3. Classification of types of modification of radio hormesis effects from the point of view of the order of action of the main (in radio hormesis dose/power) and modifying factors

Radio modification			
Preradiation		Postradiation	
Positive (increase in resistance before radiation)	Negative (decrease in resistance before radiation)	Positive (increase in resistance after radiation)	Negative (post-radiation decreases in resistance)

Table 4. Classification of types of modifications of radioprotective effects in terms of the sign (direction) of the radio modifying influence on resistance

Radio modification			
Positive		**Negative**	
Preradiation (enhancement of resistance before radiation)	Postradiation (enhancement of resistance after radiation)	Preradiation (reduction of resistance before radiation)	Postradiation (reduction of resistance after radiation)

In the study we focus in detail on one type of post-radiation positive modification of the effect of the radiation factor in inhibiting doses (in italics in Tables 1 and 2). Radiobiology is well aware of the positive post-radiation effects of incubation conditions (lowered temperature, 'starvation medium', etc.) (Korogodin, 1966). In this case, post-radiation factors create conditions for more effective/resultant work of intracellular and supracellular recovery systems. Our approach is unique in attempting to use ionizing radiation itself as a positively acting post-radiation factor. In other words, we tried to test the possibility of "treating" (providing a 'radiotherapy' effect) acutely irradiated objects with additional irradiation in the post-radiation period. In fact, we have 'turned' into a standard scheme (algorithm) for studying a radio-adaptive (more precisely, hyper-adaptive) response, when an adapting dose of ionizing radiation is applied after the so-called test dose, which has an inhibitory effect on a biological object.

In studying the effect of radio adaptation (positive pre-radiation modification), a traditional interaction scheme is employed between modifying (adapting or de-adapting) factors and test factors, where the action of the first precedes the action of the second in time. This approach covers almost all cases of prophylactic (protective) and sensitizing actions of the first impact in relation to the second, which acts as inhibitory (Myheev, Gushcha, Shilyna, 2002). Our study is based on the assumption that if the applied adapting and test factors are of similar nature (e.g., ionizing radiation in the first and second cases), they primarily act at the same level of system-object integration, implying that the effect of their joint action is independent of the order of their application.

As an adaptive effect, hormesis doses are usually used and, if it, when applied after a test effect, reduces the degree of negative influence of the test effect, then this will obviously indicate a therapeutic type of modifying influence of the adapting effect. In the biology of plant and animal resistance to stressors, this possibility (in fact, radiation 'homeopathy') has not been sufficiently studied. We studied this modification, termed 'reverse adaptation', where various impacts, including chronic ionizing radiation, served as therapeutic influences on plant subjects.

MATERIALS AND METHODS.

In experiments investigating the 'homeopathic' effect of chronic ionizing radiation, 4-day-old pea sprouts of the Kharkiv-317 variety were used. The sprouts were initially irradiated at the 'RESEARCHER' gamma installation with a dose of 6 Gy at a power of 4.2 Gy/s. The dose was chosen based on data from preliminary experiments in which it temporarily inhibited the growth activity of seedlings with subsequent recovery. Irradiated seedlings were divided into two groups, one of which served as a relative control (absolute - non-irradiated seedlings), and the second was experimental. The latter sprouts were placed under chronic gamma radiation from a water solution of cesium-137 chloride in a glass ampoule. At a 5 cm distance from the source, the gamma background power was about 500 µGy/h (0.5 mGy/h, 50 mrad/h). This power 'provided' irradiation of the object at a dose of about 1.0 cGy per day. Plants were grown in a thermostat at a temperature of 24°C, illumination intensity of 2.2 kLx and light-dark mode: 14 hours of light + 10 hours of darkness.

RESULTS AND DISCUSSION

The therapeutic (‘homeopathic’) effect of post-radiation irradiation was observed in experiments with bean, evening primrose and pea seedlings (see Fig. 1 and 2). Noteworthy (Fig. 2) is the coincidence of the dynamics of radio adaptation proper (‘adaptive response’) and ‘reverse adaptation’ obtained according to the scheme when test irradiation precedes the adapting dose.

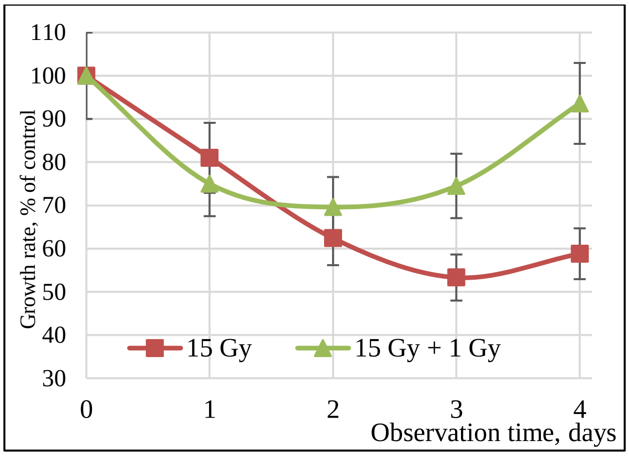


Fig. 1. Effect of acute gamma irradiation on the growth rate of the main root of bean sprouts

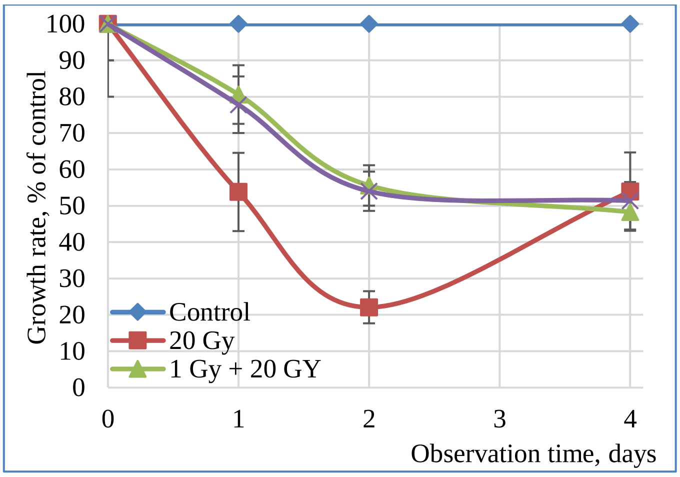


Fig. 2. The dynamics of effects from different schemes of applying acute gamma irradiation to evening primrose sprouts

Similar to direct (ordinary) adaptation, reverse adaptation was observed to have a transitive character, meaning over time, the parameters of the experimental variant approached those of the control variant. It is hypothesized that post-radiation ‘radiotherapeutic’ procedures modify the work of recovery systems in irradiated plants, creating additional opportunities for more complete recovery at the intracellular (molecular) or cell-population levels. The completion of recovery processes at a specific level, for example, at the cellular level, means the emergence of conditions for its modification even before the completion of corresponding processes at higher levels. This circumstance allows for the application, after inhibiting or even lethal exposure to the object, of impacts that would have been adapting if applied before the inhibiting test exposure. The effect of such influence is identical to the effect of the traditional prophylactic scheme, where the first dose acts as adapting (‘training’).

Particularly of interest, given the need to assess the impact of increased radiation background caused by the Chernobyl accident, was the study of ‘reverse adaptation’ when chronic ionizing radiation is used as a radiotherapeutic means. Figure 3 presents summarized data from ten independent experiments studying the ‘radiotherapeutic’ action of chronic gamma radiation. It is observed that the effect does not manifest immediately, partly explained by the gradual accumulation of absorbed dose from the source of chronic radiation. Nonetheless, the effect is clearly registered and possesses cumulative property, meaning a gradual dose accumulation, leading to the return of growth parameters to the control level (in this case, to the growth parameters of plants acutely irradiated with a dose of 6 Gy). It's evident that if observations continued under these conditions, due to further accumulation of absorbed dose under chronic irradiation, the growth activity of the experimental plants would likely be inhibited. However, it is possible that the applied power of chronic irradiation would not significantly affect subsequent growth phases of the plants. Chronic radiation exposure (see Fig. 4) has a hormetic (positively stimulating) effect on growth characteristics. This supports the similarity, and possibly the identity, of mechanisms between ‘direct’ and ‘reverse’ adaptation discussed earlier.

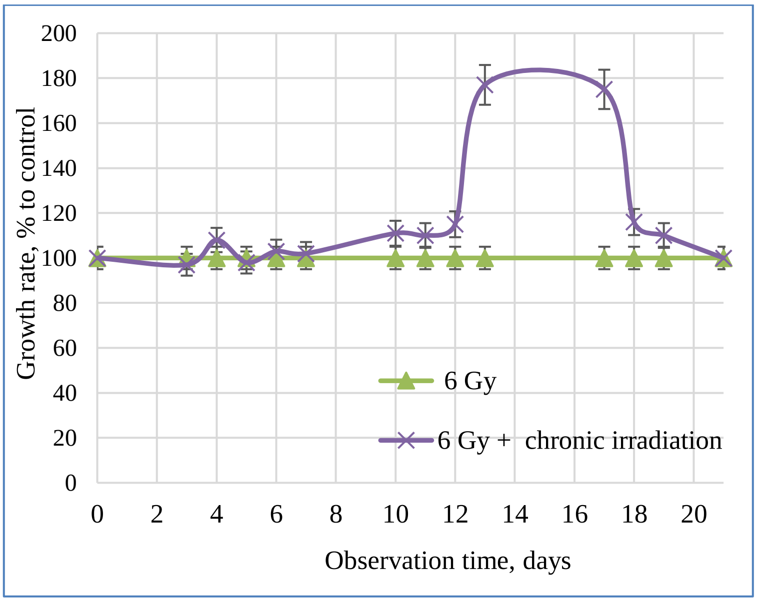


Fig 3. The impact of post-radiation conditions on the growth response of pea sprouts of the Kharkiv-317 variety. It shows plants acutely irradiated with a dose of 6 Gy compared to plants acutely irradiated with 6 Gy and then placed under the influence of a gamma radiation source with a power of 500 μGy/h.

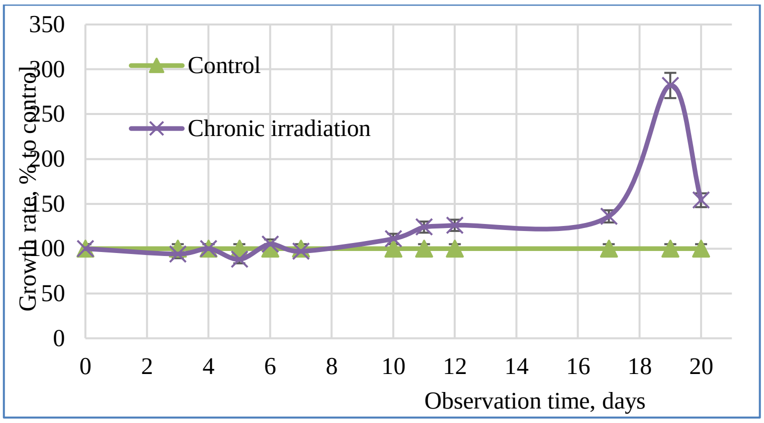


Fig. 4. The effect of chronic irradiation (500 μGy/h) on the growth response of the roots of pea seedlings of the Kharkovsky-317 variety (Control - non-irradiated plants, Chronicle - plants located in the field of action of a gamma irradiation source with a power of 500 μGy/h)

It should also be noted that the onset of the 'therapeutic' effect of chronic irradiation (8-10 days after the start of the experiment) almost coincides with the onset of the hormetic effect of chronic irradiation.

Due to technical reasons preventing long-term incubation of plants, the further fate of irradiated sprouts under chronic gamma radiation remained unclear. However, it is evident that the ultimate effect of 'chronic exposure' as a factor modifying the inhibitory effect of acute gamma irradiation would depend on its power and accumulated absorbed dose. Regardless, considering the potential nonspecific action of chronic radiation as a therapeutic means, it wouldn't be difficult to develop a methodology for its use to reduce negative effects not only of ionizing radiation but also of other chemical and biological factors. While factors of any nature can be used for therapeutic impact, as previously mentioned, we emphasize the somewhat paradoxical statement that radiation damage can be minimized using radiation effects, of course, in appropriate doses or powers of ionizing radiation.

Thus, the presented results suggest an experimental basis for a 'low-dose radiotherapy' method which may find its application in treating acute radiation sickness.

REFERENCES

[1] Grodzinsky D. M., Gudkov I. N. (1973). Protection of plants from radiation damage. M.: Atomizdat, p.232 (in Russian).
[2] Korogodin V. I. (1966). Problems of post-radiation recovery. M.: Atomizdat, 312 (in Russian).
[3] Kuzin A. M. (1977). Ideas of radiation hormesis in the atomic age. M.: Nauka, 137 (in Russian).
[4] Mikheev A. N. (2015). Hyper-adaptation. Stimulated ontogenetic adaptation of plants. K.: Phytosociocenter, p.423 (in Russian).
[5] Mikheev O. M., Gusha M. I., Shilina Yu. V. (2002). Endogenous and exogenous factors in the implementation of the phenotypic adaptation potential of plants (theoretical and experimental aspects). On Sat. Physiology of growing plants in Ukraine for thousands of years. Vol. 2, 82 – 87 (in Ukrainian).
[6] Rozhdestvensky L. M. (1985). Mechanisms of the radioprotective effect and indication of the effectiveness of radioprotectors. M.: Energoatomizdat, 125 (in Russian).
[7] Selye G. (1982). Stress without distress. M.: Progress, 1982. 128 (in Russian).