Ionizing Radiation and Hormesis. What is the Risk of Cancer at Low Doses?

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Abstract

The risk of radiogenic cancer remains elusive epidemiologically at absorbed doses below about 100–200 mSv. To overcome this uncertainty in the effort at optimal protection of radiation-exposed people against late effects such as cancer,the assumption was made that cancer risk rises linearly with absorbed dose, i.e., according to the Linear-no-Threshold (LNT) hypothesis. However, over the past decades many experimental datain cells, tissues and animals were not compatible with this hypothesis. The data rather indicate low-dose-induced non-linear system responses that are not seen at high doses and encompass by-stander effectsand adaptive protection.

In summarizing the current state of research, primary radiation effects and biological system responses need be both considered. Ionizing radiation primarily perturbs the basic molecular level proportional to dose, with potential damage amplification at this level and propagation to higher levels: cells, tissues, organs, and whole body. Genomic instability is an example of late damage amplification. Three types of defenses operate against such damage and its propagation, one physical and two metabolic ones. The physical type of barrier appears to be inherent at defined system sites where a certain impact threshold needs be overcome to cause damage and propagation. There are two subsequent metabolicdefenses, of which one acts immediately and involves, under individual genetic control, scavenging of toxins; – molecular repair, especially of DNA; – removal of damaged cells either by apoptosis, necrosis, phagocytosis, cell differentiation-senescence, or by immune responses, – followed by replacement of lost system elements. Aspectrum of second metabolicdefenses appearswith a time delay. They embraceup-regulations of immediately operating defense mechanisms. Such so-called adaptive protections may function beyond a year and have target-specific maxima after single tissue absorbed doses around 100 to 200 mSv and most do not appear at doses above about 500 mSv. – These temporarily operating protectionsdefend not only against effects of renewed exposure to the primarily acting radiation but also against impactsfrom non-radiogenic toxins that mimic radiation effects. Adaptive protections may arise also at low dose-rates with repetitive energydepositions occurring at certain time intervalsin individual cells.

Low-dose-risk modeling must recognize the balance between radiogenic cancer induction and up-regulation of protection against spontaneous cancer. Adaptive protectionsthat prevent only about 2–3 % of the life-time risk of spontaneouscancer would already fully balance an assumed LNT-based radiogenic cancer risk at about 100 mSv, in agreement with epidemiological data. The probability of adaptive protection against spontaneous cancerat low doses and dose-rates determines the overall cancer risk in the exposed population¸ which may become lower than the spontaneous cancer risk – a hormetic effect that conforms with epidemiological data and invalidates the LNT hypothesis.