Implementation Issues in Inherent Radio Sensitivity by Regulation of Chromatin Access

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Abstract

From physical agents used in the most dangerous health field are the Ionizing radiation may be used in medical diagnosis and treatment. Its effects on people may have consequences for their health or the health of future generations (somatic and genetic risks), so it is essential for staff meet sanitary measures radiation protection in the workplace in which using these radiations. We also have to know the permitted maximum allowable dose exposed for professionals and the public in general, possess a system Personal dosimetry for professionals who are in contact with radiation ionizing and observance of the warning signs or risk of radiation.

Index Terms— Fanconi anemia, radio protectors, GS-nitroxide, clinical radio sensitivity

I. INTRODUCTION

Radiation can be classified according to the effects it produces on matter, into ionizing and non-ionizing radiation. Ionizing radiation includes cosmic rays, X-rays and the radiation from radioactive materials. Non-ionizing radiation includes ultraviolet light, radiant heat and microwaves. The word radiation is commonly used in reference to ionizing radiation only (i.e., having sufficient energy to ionize an atom), but it may also refer to non-ionizing radiation (e.g., radio waves or visible light). The energy radiates (i.e., travels outward in straight lines in all directions) from its source. This geometry naturally leads to a system of measurements and physical units that are equally applicable to all types of radiation. Both ionizing and non-ionizing radiation can be harmful to organisms and the natural environment. All life on Earth has evolved in presence of this radiation. Figure 1.1 shows the percentage contribution of various sources of ionizing radiation to which human beings are exposed. Over 85 percent of total exposure is from natural resources with about half coming from radon decay products in the home. Medical exposure of patients accounts for 14 percent of the total, whereas all other artificial sources – fallout, consumer products, occupational exposure, and discharges from nuclear industries account for less than 1 percent of the total value. Of all the exposures, medical exposure is of the main interest to scientists all over the world because of the ability of radiation to treat dreaded disease like cancer, for which, ironically it is a cause as well.

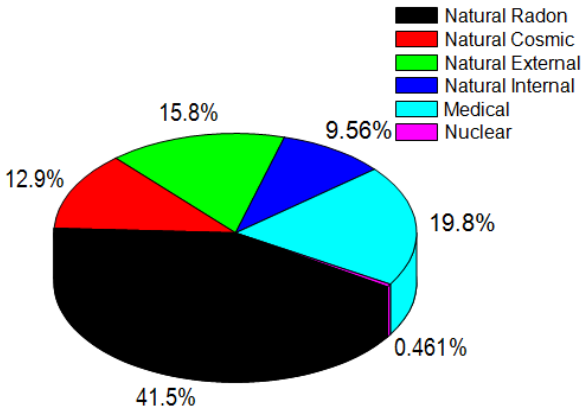

Fig.1 Pie-chart showing the percentage of radiation exposure from various sources.

Whenever the energy of a particle or photon exceeds the ionizing potential of a molecule, a collision with the molecule might lead to its ionization. Therefore, ionizing radiation, upon interaction with matter, has an ability to remove electrons from atoms resulting in the formation of ions. The result of this interaction is the production of negatively charged free electrons and positively charged ions and hence the term "ionizing radiation". In other words it can be described as radiation is considered to be ionizing, if it has a wavelength <10-6 cm. Such a radiation has sufficient energy in an individual photon to eject orbital electrons from a molecule or atom. Ionizing radiation can be broadly classified into electromagnetic (X-rays and γ-rays) and particulate (electrons, neutrons, protons, α particles, heavy ions etc.). Electromagnetic radiations, as the name implies, are made up of an electric and a magnetic component. They carry energy but have no charge or mass. While electromagnetic radiations form a broad spectrum of energies, the ionizing component i.e. X-rays and γ-rays comprise the high energy end of the spectrum (wavelength below 200 nm). The particulate constituent has both mass and energy. They can be further subdivided into charged particles (electrons, neutrons, protons, α particles), which bear a positive or negative charge and uncharged particles which bear no charge (neutrons) [1]. Radiation can also be classified in terms of their linear energy transfer (LET)

II. RADIATION INDUCED BY STANDER SIGNALING

In recent years, the advancement of medical technologies is fostering an unstoppable rise in techniques using radiation, which is very necessary knowledge for all health professionals such physical agents that are used in all fields of health work and especially the risks to which people may be subjected (health professional or otherwise) that may be in contact with such agents in their work environment, because if radiation
ionizing penetrate living tissues, can cause significant biological effects. Therefore, it is necessary to know what are the biological effects of this radiation and know the risks, doses and protective measures with regard to the legislation by those who work in contact with ionizing radiation or places used, as in the health care and proliferate those sources.

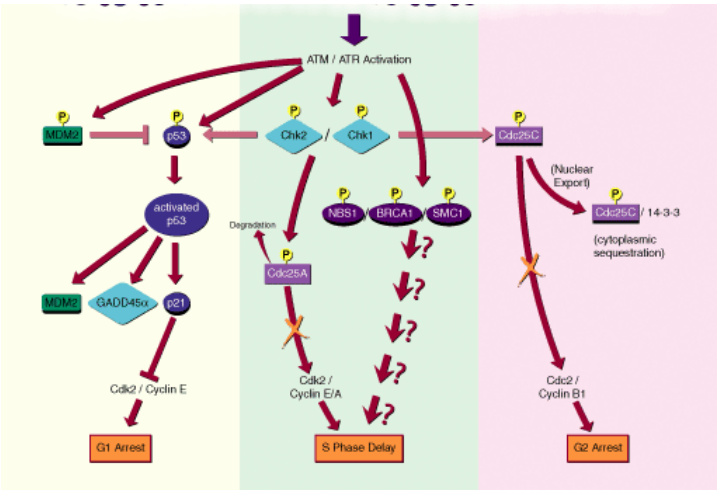

Fig. 2: Regulation of Cell Cycle by p53 and p21.

That's why throughout this chapter, we discuss what physical agents are which of them are radiation, which are ionizing radiation, what are used in the health field and what the risks or undesirable effects of radiation on the human body and what dose of radiation can be produced are, to end with the concepts and standards radiation protection must observe and enforce health in contact in their work environment with these physical agents and existing legislation in this regard.

III. METHODOLOGY

Physical agent radiation is transmitted through the space without any contact between the source output and the application object. Examples of radiation of X-rays, gamma rays, heat (infrared radiation) or light. These cited in addition electromagnetic radiation may be considered, because they are associated with wave electric and a magnetic field and a radiation energy different to others, and all have the speed of light. We can also divide the radiation and in general to all physicists in ionizing and non-ionizing agents. The ionizing radiation is directly can themselves cause ionizations boot ie electrons from atoms that form the field application or the tissue to interact, converting those atoms were neutral to charged ions. The ionization mechanism is an alteration biological caused by radiation, which can subsequently lead to disturbances chemical and these lead to more or less important biological changes. Are direct ionizing radiation of electron beams or protons, or in general charged particles. We understand that vehicle physical agent or an energy carrier when absorbed by living things can cause a biological effect on them. They can be examples of physical agents X-rays, gamma rays, ultrasound, heat, light and even the movement and massage, because they all have in common that are energy vehicles that can cause biological effects in organisms alive. Some physical agents are radiation.

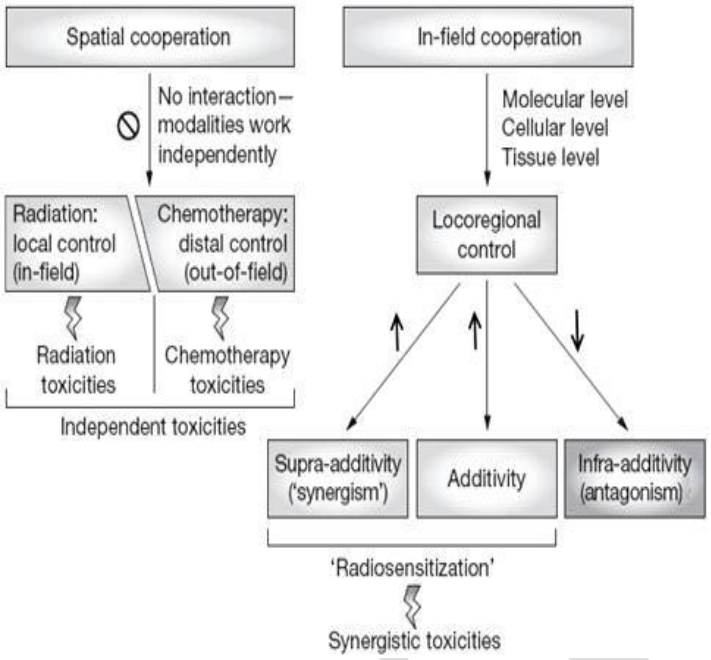

Figure 3. Rationale for adding chemotherapy to radiation.

It is now increasingly believed that combining ionizing radiation with cytotoxic chemotherapy results in better tumor control rates, both within the target volume and potentially also at distant microscopic sites. The introduction of combined modality approaches was a highly significant step in the evolution of curative radiation treatment. Three clinical rationales support the use of combined modality approach involving chemotherapy and radiation. First, concomitant chemo radiotherapy can be used with organ-preserving intent, resulting in improved cosmesis and function compared with surgical resection with or without adjuvant treatment. Second, chemotherapy can act as a radio sensitizer, improving the probability of local control and, in some cases, survival, by aiding the destruction of radio resistant clones. Third, chemotherapy given as part of concurrent chemo radiation may act systemically and potentially eradicate distant micro metastases. A number of factors including drug type, concentration, drug target, metabolism, timing of administration, micro-environmental and genetic factors, etc. are known to influence the efficacy of the combined modality treatment. In several common solid tumor types, landmark clinical studies have clearly demonstrated the benefit of combined modality treatment and the number of patients undergoing such treatment has been increasing steadily for the last two decades.

IV. RESULT

It is long-established that plants possess diverse principles, which are of immense nutritional and medicinal value. Numerous anticancer screening studies have been conducted using traditional medicinal plants in an attempt to discover new therapeutic agents that are devoid of toxic side effects generally known to be associated with current chemotherapeutic agents. Currently, research is focused more on developing anti-cancer drugs and their derivatives isolated from natural sources, especially phytochemicals with improved anticancer potential and minimal systemic toxicity. Naturally occurring quinines represent a large group of quinoa compounds that are known to possess a spectrum of pharmacological activities, including anticancer activity although, there are many clinically important anticancer agents containing Quinone nucleus many other quinines are still being tested for

their anticancer activity. Among the natural compounds, plant- derived quinines have been extensively studied for their potential as cytotoxic/anticancer agents. Plumbagin (5- hydroxy-2-methyl-1, 4-napthoquinone) derived from the roots of is one such compound. Earlier studies have given sufficient insight into the anticancer and radio sensitizing properties. Besides, other natural The chapter discusses various MAC technologies in context to multi - channel MAC protocols to cognitive radio technology based MAC protocols .

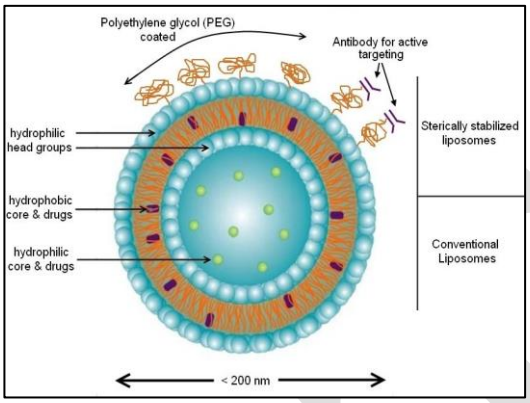

Figure 4. Diagram of a drug- loaded liposome both with and without a P EG coating.

Ultimately, ionizing physical agents are those that can produce ionizations ie pair formation (positive and negative) ions electron stripping bark atoms, and physical agents not ionizing are those who do not have that capability.

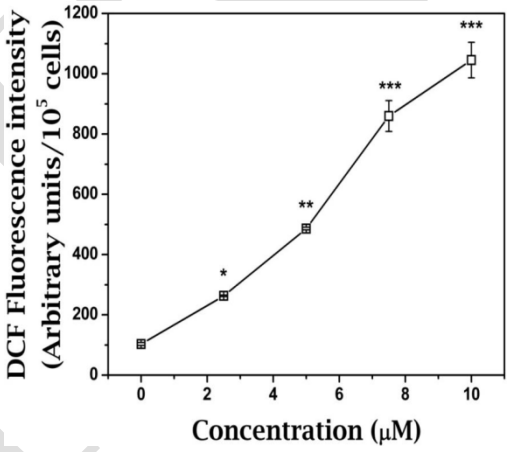

Figure 5. Effect of treatment on the intracellular ROS levels

A physical agents ionizing they called ionizing radiation. From the viewpoint of radiation exposure are more dangerous the ionizing radiation, because they can produce greater biological effects, and will have to be more careful in protecting against them. Examples of ionizing radiation used in the health field, X-rays and gamma rays, which are used both for diagnosis and treatment and the research.

V. DISCUSSION AND CONCLUSION

The irradiation of cells with fractionated doses led to a signaling response that was different from a single dose of irradiation. A549 cells were found to be relatively more radio resistant if the 10Gy dose was delivered as a fractionated regimen. Microarray analysis showed up

regulation of DNA repair and cell cycle arrest genes in the cells exposed to fractionated irradiation. There was intense activation of DNA repair pathway (DNA-PK, ATM, Rad52, MLH1 and BRCA1), efficient DNA repair and phospho-p53 was found to be trans located to the nucleus of A549 cells exposed to fractionated irradiation. MCF-7 cells responded differently in fractionated regimen. Silencing of the Rad52 gene in fractionated group of A549 cells made the cells radiosensitive. The reasons for the radioresistance of the A549 cells lay in the repair pathway, the Rad52, the inhibition of which could revert the cells to radio sensitivity leading to a decrease in survival.

Proton beam was found to be more cytotoxic than γ-radiation. Proton beam irradiated cells showed phosphorylation of H2AX, ATM, Chk2 and p53. The mechanism of excessive cell killing in proton beam irradiated cells was found to be up regulation of Box and down-regulation of Bcl-2. The noteworthy finding of this study is the biphasic activation of the sensor proteins, ATM and DNA-PK and no activation of ATR by proton irradiation. Carbon beam was found to be three times more cytotoxic than γ-radiation despite the fact that the numbers of γ-H2AX foci were same. Percentage of cells showing ATM/ATR foci were more with gamma however number of foci per cell were more in case of carbon irradiation. Large BRCA1 foci were found in all carbon irradiated cells unlike gamma irradiated cells and pro-survival ERK pathway was activated after gamma irradiation but not carbon. The noteworthy finding of this study is the early phase apoptosis induction by carbon ions. Despite activation of same repair molecules, differences in low and high LET damage responses are due to distinct macromolecular complexes of repair proteins such as ATM, BRCA1 etc rather than their individual activation and the activation of cytoplasmic pathways such as ERK.

Oxygen beam was found to be three times more cytotoxic than γ-radiation. By 4h there was efficient repair of DNA in A549 cells exposed to 2Gy or 6Gy gamma radiation but not in cells exposed to 2Gy oxygen beam as determined by γ-H2AX counting. Number of ATM foci was found to be significantly higher in cells exposed to 2Gy oxygen beam.

Percentage of cells showing ATR foci were more with gamma however number of foci per cell were more in case of oxygen beam. Oxygen beam irradiated cells showed phosphorylation of Chk1, Chk2 and p53. Many apoptotic nuclei were seen by DAPI staining in cells exposed to oxygen beam. The noteworthy finding of this study is the activation of the sensor proteins, ATM and ATR by oxygen irradiation and the significant activation of Chk1, Chk2 and p53 only in the oxygen beam irradiated cells.

The current study is a clear evidence of radiation induced bystander effect being involved in adaptive responses in the bystander cells. Moreover, it also points towards the potential involvement of signaling molecules released into the medium by the irradiated cells which elicit a response in the bystander cells. Also there may be potential involvement of stable free radicals that are produced in the medium as a result of irradiation, in eliciting a response from the bystander cells. The mechanism of which may be via NO generation.

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