EFFECT OF RADIATION ON DNA

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Abstract

Ionizing radiation (X-rays) are a type of high-energy electromagnetic radiation that can interact with living tissue, including DNA molecules. The interaction of x-rays with DNA can lead to a range of biological effects, some of which can be harmful.

When x-rays pass through living tissue, they can ionize atoms and molecules, causing the formation of free radicals. These free radicals can then react with and damage the DNA molecule, leading to breaks in the DNA strands and other types of damage.

The extent of the damage caused by x-rays depends on a number of factors, including the energy of the x-rays, the intensity and duration of the exposure, and the type of tissue being exposed. Higher energy x-rays and longer exposures generally lead to more extensive damage to the DNA.

One of the most significant effects of x-ray exposure on DNA is the induction of mutations. Mutations are changes in the genetic code that can alter the normal functioning of cells and potentially lead to the development of cancer. X-rays can cause mutations by directly damaging the DNA molecule or by interfering with the normal DNA repair mechanisms in the cell.

Another effect of x-ray exposure on DNA is the induction of cell death. If the damage to the DNA is severe enough, the cell may undergo programmed cell death, or apoptosis, to prevent the propagation of potentially harmful mutations.

Despite the potential for harmful effects, low levels of x-ray exposure are commonly used in medical imaging procedures, such as X-ray .These procedures use low doses of x-rays to create images of the inside of the body, allowing doctors to diagnose and monitor a variety of conditions. While there is a small risk associated with radiation exposure, the benefits of these procedures generally outweigh the risks.

In conclusion, x-rays can have a range of effects on DNA, including the induction of mutations and cell death. The extent of these effects depends on a variety of factors, including the energy of the x-rays and the duration and intensity of the exposure. While low levels of x-ray exposure are commonly used in medical imaging, it is important to minimize unnecessary exposure to radiation to reduce the risk of harmful effects

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INTRODUCTION

RADIATION

Radiation is small pockets of energy, which travel as waves and transfer energy from one point to another point. There are two types of radiation namely: (i) photons, e.g. X, gamaand (ii) particles, e.g. e, p, n and alpha. Radiation is a double edged weapon, analogous to fire, which possesses both benefits and hazards. Radiation hazards were witnessed by the following events in early days:

1. Uranium mine workers
2. Atomic bomb explosion-Hiroshima and Nagasaki
3. Radiobiology experiments.[1]

Radiation was used in medicine immediately after the discovery of X-rays by W.C. Roentgen on November 15, 1895. It was used in India in 1898 within 3 years of its discovery. The Indian army employed hefty porters to carry the cargo,(100 bounds) on a pole for 200 miles in the Hyber pass region (Pakistan). That cargo had the first X-ray tube used in India. Major Bewoor used it effectively in the North-West frontiers. The civilian use of X-rays in India began in 1900 at the Government General Hospital, presently the Barnard institute of Radiology and Oncology, Chennai.[2]

Radiation hazards were realized in the beginning of the 20th century. The X-rays were used indiscriminately in the early years and have caused visible damage to several physicians and X-ray enthusiasts. Within 6 months of their use, several cases of erythema, dermatitis and alopecia were reported among X-ray operators and their patients. In 1902 the first X-ray induced skin cancer was reported. In 1921 Ironside Bruce, a pioneering radiologist in a London Hospital died of cancer at the age of 38. Similarly several lives were lost due to excessive X-ray exposures.[3]

In 1915, the British Roentgen Society made the first radiation protection recommendations. To regulate the safe use of radiation the “British X-ray and Radium protection committee” was formed (1921). It was made an International Committee in 1928 and later (1950) transformed as “International Commission on Radiological Protection”(ICRP). The ICRP is the first standard setting body formed, for the purpose of radiological safety. The similar organization in the USA is the National council on radiation protection and measurements (NCRP), which was formed in 1946.[4]

SOURCES OF RADIATION

The sources of radiation are classified into

(i) Natural radiation sources,
(ii) Enhanced natural sources,
(iii) Artificial radiation sources (man-made) and
(iv) Occupational exposures.

The annual average per capita total effective dose equivalent is 3.6 mSv (NCRP-93,US data). About 82% of the above exposure (3 mSv) arise from naturally occurring sources, 18% (0.6 mSv) arise from technological enhancements of naturally occurring sources and artificial radiation sources (diagnostic X-ray is the major contributor). Background radiation involves both natural and man-made low level radiation exposure to all members of the public. This will vary with region and Kerala and Brazil have high background levels of radiation (100 mSv/year).[5]

Natural Radiation Source

The natural radiation sources includes
Cosmic rays,
(ii) Terrestrial (Primordial) radionuclides, and
(iii) Internal Radioisotopes.

Cosmic Rays

Cosmic rays are extraterrestrial radiation that strikes the earth’s atmosphere that includes primary and secondary. Primary cosmic rays, in which protons account for 80%. The primary cosmic rays collide with the atmosphere, producing showers of secondary particles (electrons, muons) and electromagnetic radiation. The average per capita equivalent dose is 270 mSv per year, which makes 8% of the natural background.

Cosmic exposures increase with altitudes. It is estimated that at 30,000 ft altitude the equivalent dose is about 5 mSv per hour and it is doubling in every 1500 feet. It is greater at the earth poles than the equator. Structures provide some protection against cosmic rays, and hence the indoor effective dose is 20% lesser than outdoor.

Air travel increases an individual's cosmic ray exposures. Air crews and frequent fliers receive an additional annual equivalent dose of 1mSv. A 5 hr transcontinental jet aircraft travel result in 25 mSv equivalent dose.

Apollo astronauts received an average equivalent dose of 2.75 mSv during the lunar mission. A part of secondary cosmic ray particles collide with stable atmospheric nuclei and produces cosmogenic radionuclides; e.g.147 N (n,p) 146 C, but their contribution to natural background is very

little.[6]

Terrestrial Radiations

Terrestrial radionuclides that have been present on earth since its formation are called primordial radionuclides. Their physical half-lives are comparable to the age of the earth (4.5 billion yeras). Their decay products are the major contributors of terrestrial radiations. They mainly contribute in the form of external exposure, inhalation, and ingestion.[9]

External exposure: K-40,U-238, and Th-232 are mainly responsible for external exposure and they account an equivalent dose of 280 mSv per year. This may vary depending upon the local concentration of terrestrial radionuclides. Inhalation: Rn-222 (U-238) is a noble gas, decays to polonium-218 by alpha emission with half-life of 3.8 days. Its decay products are the most significant source of inhalation exposure. It is deposited in the tracheobronchial region of the lung. Radon concentration varies widely both seasonal and diurnal. It emanates from sail and is restricted by structures. Weatherproofing of homes, energy conservation techniques, decreased ventilation are resulting in higher indoor radon concentration. Radon inhalation accounts for an equivalent dose of 2 mSv/year to the bronchial epithelium. It accounts for about 55% of natural background, which can be easily measured and reduced.

Ingestion: Ingestion of food and water is the second largest source of natural background in which K-40 is the most significant. It is a naturally occurring isotope of potassium having higher concentration at the skeletal muscle. It accounts an average equivalent dose rate of 400 mSv/year.[7]

Internal Radionuclides

Internal radionuclides include K-40 and C-14, which are present in the human body. The main contributor is K-40, which emits □ and □ rays and decays with a half-life of 1.3 × 109 years.

Enhanced Natural Sources

Enhanced natural sources mainly consist of consumer products. The largest contributor is tobacco products, which burdens the bronchial epithelium. It produce an effective dose equivalent of 2.8mSv/year.

Radon gas dissolved in domestic water supply can contribute 10-60 mSv/ year. Building materials consists of uranium, thorium and potassium and these are present in brick, concrete, granite which may contribute an annual effective dose of 30 mSv /year. Mining and agricultural activity contribute to a lesser level by fertilizers (uranium, thorium decay products and K-40).Combustible fuels including coal, natural gas and consumer products includes smoke alarms (americium-241), gas lantern mantles (thorium), dental prostheses, certain ceramics, optical lenses (uranium) contribute <1% annual effective dose [8]

Artificial Sources

The artificial sources of radiation includes medical exposure, radioactive10 fallout, nuclear power and occupational exposure.

Medical Exposure

The majority of the exposure is from medical X-rays (Fluoroscopy & Computed tomography) which contribute to 58% of the artificial radiation exposure. Next contributor is the nuclear medicine which is 21%. Both produces an annual average effective dose equivalent of 540 □Sv per year. It accounts for about 69% of artificial radiation.

Consumer Products

It accounts for 16% of the artificial radiation exposure. Substances in consumer products such as tobacco, the domestic water supply, building materials, and to a lesser extent, smoke detectors, televisions, and computer screens, account for the above exposures.

Radioactive Fallout

It arises from atmospheric testing of nuclear weapons and consists of Carbon-14 (70%) and other radionuclides including H-3, Mn-54, Cs-136, 137, Ba-140, Ce-144, plutonium and Trans plutonium elements. It results in an annual effective dose equivalent of <10mSv. It contributes 2% of the manmade radiation exposures.

Nuclear Fuel Cycle

The contribution from nuclear power production is very minimal, which is about 1% of artificial radiation (Annual effective dose is <0.5mSv). It involves all phases of the fuel cycle; mining, manufacturing, reactor operations, and waste disposal. The most significant contributor is Carbon-14.[9]

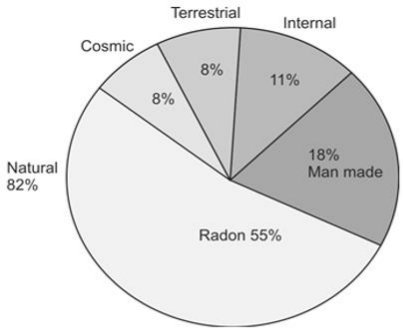
Occupational Exposure

The occupational exposures associated with uranium mining (12 mSv per year), nuclear power operations, medical diagnosis and therapy, aviation and research, non-uranium mining, and application of phosphate fertilizers. It contributes about 2 % of the artificial radiation exposure.

Radiologist, X-ray technologist receive an average annual effective dose of 1 micro-Sv. However special procedures involving fluoroscopy and cine-radiology (e.g. cardiac catheterization) may exceed 15 mSv. These are only partial body exposures (head & extremities), if lead apron is used during the procedure. The UNSCEAR and the NCRP have published the global annual dose contribution from various sources of radiation.

The average annual effective dose equivalent to a population from all radiation sources, is obtained by dividing the annual collective effective dose equivalent by the size of the population.

Medical use of radiation warrants an optimal compromise between clinical utility and radiation dose to patients, staff and the public. The success of radiation protection mainly lies on the education of staff. They should be educated on radiobiology, genetics, risk analysis, methods of reducing radiation dose, decay patterns of radioactivity released in the environment and absorbing power of different materials to different radiation.



The % contribution of various types of man-made sources to the total average effective dose equivalent to the US population

Table 1.5: Annual occupational effective dose equivalent (US Data)

Category	*Average annual total effective dose equivalent (mSv)*
Uranium miners	12.0
Nuclear power operations	6.0
Airline crews	1.7
X-ray and Nuclear Medicine technologists	1.0
Radiologists	0.7

CELL

Cell is the basic unit of life. Living organisms are made up of either a single cell or many cells. Human beings are multicellular organisms built up of 10-14 cells. Cell consists of a nucleus, which is surrounded by a viscous liquid known as cytoplasm. Both the cell and cytoplasm are enveloped by a membrane, which is known as cell membrane or plasma membrane.

The constituents of cytoplasm control the functions of the cell. The nucleus contains tiny thread like structures known as chromosomes, which are made up of deoxyribonucleic acid (DNA) and protein. The DNA molecules contain all the information required for the cellular function in coded form and thus control the nature and growth of the individual. Sections of chromosomes, which contain information for specific functions, are called genes. Cells of similar nature constitute a tissue and different tissues form an organ. Many organs constitute a system (like respiratory system, digestive system, hematopoietic system and nervous system).

Cells are mainly classified into two categories:
(i) somatic cells, and
(ii) reproductive (or germ) cells.

Somatic cells constitute various tissues such as skin, liver, brain etc. Germ cells are those, which participate in the reproductive process. They are sperm in males and ovum in females. All somatic cells in the human body contain 46 chromosomes as 22 pairs and two sex determining chromosomes. Reproductive cells contain only 23 chromosomes.[10]

DNA

DNA is the information molecule. It stores instructions for making other large molecules, called proteins. These instructions are stored inside each of your cells, distributed among 46 long structures called chromosomes. These chromosomes are made up of thousands of shorter segments of DNA, called genes. Each gene stores the directions for making protein fragments, whole proteins, or multiple specific proteins.

DNA is well-suited to perform this biological function because of its molecular structure, and because of the development of a series of high performance enzymes that are fine-tuned to interact with this molecular structure in specific ways. The match between DNA structure and the activities of these enzymes is so effective and well-refined that DNA has become, over evolutionary time, the universal information-storage molecule for all forms of life. Nature has yet to find a better solution than DNA for storing, expressing, and passing along instructions for making proteins.[11]

THE MOLECULAR STRUCTURE OF DNA

In order to understand the biological function of DNA, you first need to understand its molecular structure. This requires learning the vocabulary for talking about the building blocks of DNA, and how these building blocks are assembled to make DNA molecules.

DNA molecules are polymers. Polymers are large molecules that are built up by repeatedly linking together smaller molecules, called monomers. Think of how a freight train is built by linking lots of individual boxcars together, or how this sentence is built by sticking together a specific sequence of individual letters (plus spaces and punctuation). In all three cases, the large structure—a train, a sentence, a DNA molecule—is composed of smaller structures that are linked together in non-random sequences— boxcars, letters, and, in the biological case, DNA monomers. DNA monomers are called nucleotides

Just like a sentence "polymer" is composed of letter "monomers," a DNA polymer is composed of monomers called nucleotides. A molecule of DNA is a bunch of nucleotide monomers, joined one after another into a very long chain. There are four nucleotide monomers
The English language has a 26 letter alphabet. In contrast, the DNA "alphabet" has only four "letters," the four nucleotide monomers. They have short and easy to remember names: A, C, T, G. Each nucleotide monomer is built from three simple molecular parts: a sugar, a phosphate group, and a nucleobase. (Don't confuse this use of "base" with the other one, which refers to a molecule that raises the pH of a solution; they're two different things.)The sugar and acid in all four monomers are the same

All four nucleotides (A, T, G and C) are made by sticking a phosphate group and a nucleobase to a sugar. The sugar in all four nucleotides is called deoxyribose. It's a cyclical molecule—most of its atoms are arranged in a ring-structure. The ring contains one oxygen and four carbons. A fifth carbon atom is attached to the fourth carbon of the ring. Deoxyribose also contains a hydroxyl group (-OH) attached to the third carbon in the ring.[12]

The phosphate group is a phosphorus atom with four oxygen atoms bonded to it. The phosphorus atom in phosphate has a marked tendency to bond to other oxygen atoms (for instance, the oxygen atom sticking off the deoxyribose sugar of another nucleotide).

The four nucleotide monomers are distinguished by their bases.
Each type of nucleotide has a different nucleobase stuck to its deoxyribose sugar.
A nucleotide contains *adenine.*
T nucleotide contains *thymine*
G nucleotide contains *guanine*
C nucleotide contains *cytosine*

All four of these nucleobases are relatively complex molecules, with the unifying feature that they all tend to have multiple nitrogen atoms in their structures. For this reason, nucleobases are often also called *nitrogenous* bases.

Phosphodiester bonds in DNA polymers connect the 5' carbon of one nucleotide to the 3' carbon of another nucleotide. The nucleotide monomers in a DNA polymer are connected by strong electromagnetic attractions called *phosphodiester bonds*. Phosphodiester bonds are part of a larger class of electromagnetic attractions between atoms that chemists refer to as covalent bonds.

Chromosomes are made of two DNA polymers that stick together via non-covalent hydrogen bonds Chromosomal DNA consists of two DNA polymers that make up a 3-dimensional (3D) structure called a double helix. In a double helix structure, the strands of DNA run antiparallel, meaning the 5' end of one DNA strand is parallel with the 3' end of the other DNA strand.[13]

The nucleotides forming each DNA strand are connected by noncovalent bonds, called hydrogen bonds. Considered individually, hydrogen bonds are much weaker than a single covalent bond, such as a phosphodiester bond. But, there are so many of them that the two DNA polymers are very strongly connected to each other.

THE BIOLOGICAL FUNCTION OF DNA
DNA polymers direct the production of other polymers called proteins.
A protein is one or more polymers of monomers called amino acids. Proteins are the workhorse molecules in our cells. They act as enzymes, structural support, hormones, and a whole host of other functional molecules. All traits derive from the interactions of proteins with each other and the surrounding environments. A chromosome consists of smaller segments called genes. Chromosomes are very long structures consisting of two DNA polymers, joined together by hydrogen bonds connecting complementary base pairs. A chromosome is divided into segments of double-stranded DNA called genes. Earlier, we compared a DNA polymer to a sentence, and the nucleotide monomers that make up a polymer to the letters of the alphabet that are used to write sentences down. Now that we know what genes are, and what codons are, we can extend this analogy a bit further, and begin to get an insight into how DNA stores biological information. If nucleotides are like letters, then codons are like words. Unlike English, where we use 26 letters to make words of all

different lengths and meanings, your cells use the four DNA nucleotide monomers to make "words"—codons—of just one length: three nucleotides long. If you do the math, you'll see that this means that there are just 64 possible "words" in the DNA language—64 different ways of arranging the four DNA nucleotides into three-nucleotide-long combinations.

Just like in English, where each word is associated with a dictionary definition, the codons of the DNA language are each associated with specific amino acids. During translation on the ribosomes, each codon from the original DNA gene is matched with its corresponding amino acid (with the help of tRNA molecules). Just like a human reader puts the definitions of words together to arrive at the meaning of a sentence, a ribosome puts the amino acids referred to by each codon in a gene together, creating covalent bonds between them to make a protein.
The genes that specify how to make each of the four proteins are split across two chromosomes. This means that each chromosome consists of two genes. Since the proteins specified by the genes all have four amino acid monomers, each gene must have four codons. And, since a codon always consists of three nucleotides, each gene contains 12 nucleotide monomers, and, therefore, each chromosome is 24 nucleotides long.[14]

INTERACTION OF RADIATION WITH TISSUE

Radiation deposits energy in tissues randomly and rapidly (<10-10 Sec) via excitation, ionization and thermal heating, in turn produces moving electrons. These electrons interact with atoms and molecules leading to chemical and molecular changes. These changes may appear as biological effects such as chromosome breakage, cell death, oncogenic transformation and acute radiation sickness. These effects appear after a period of time (latent period), which may vary from minutes to years. Major portion of the radiation energy appear as heat, with little biologic significance.

Radiation interactions that produce biologic effects are classified as direct and indirect action. In direct interaction, the radiation ionizes or excites the molecules such as DNA, RNA and protein directly. It involves rupture of cell membrane and break of chromosome structure, resulting in DNA strands breaking. The fragments of chromosomes produced in a direct interaction, can join together to form chromosomes with abnormal structures. This is known as chromosomal aberration. The frequency of chromosomal aberrations increases with the radiation dose and hence the magnitude of aberrations is a biological indicator of radiation dose absorbed in the human body. Chromosomal aberration analysis (CAA) is useful in determining the radiation dose received by a person who is accidentally exposed to high radiation dose (>100 mGy).

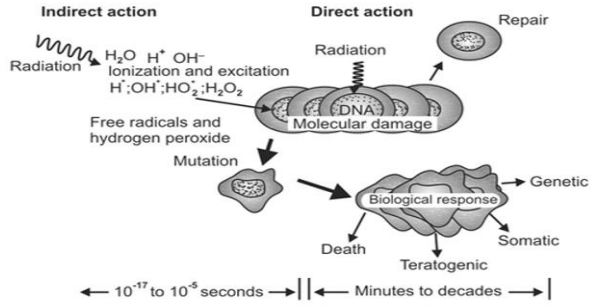
In indirect mode, the radiation interacts with the medium and produces radicals which in turn interact with the target molecule. For example, radiation interacts with oxygen and water molecules present in the cell. These interactions produce a large number of free radicals, which are uncharged atoms or molecules with an unpaired electron and hence are highly reactive. Human body tissue is composed of 70-85% water, and the major interaction (three-fourth) is indirect action. The X- rays and gamma rays effects in macromolecules of living system are mainly due to indirect interactions.[15]

The absorption of radiation by a water molecule (radiolysis) results in ion pairs (H2O+, H2O–), which are unstable and forms free radicals H* (hydrogen) and OH* (hydroxyl) as follows:
H_2O + H2O+ + H_2O– (ion pairs) H_2O+ OH+ + OH* H_2O– O H*+ OH–

OH* + OH* = H_2O_2 (hydrogen peroxide) H* + O2 = HO_2* (Hydroperoxyl radical)Free radicals are extremely reactive chemical species and perform variety of reactions.

They act as strong oxidizing or reducing agents by combining with macromolecules. For example, free radicals interfere with cell functions and may inactivate cellular mechanisms or break DNA bonds. The damaging effects of free radicals are enhanced with the presence of oxygen. In the case of low LET radiation, free radicals are the primary agents that cause the biologic effects. Approximately two-third of all radiation induced damage is considered to be caused by the hydroxyl free radical.

Repair mechanisms exist within cells which repair the cells and return to pre pre-irradiated state. For example DNA single strand break, base damage can be repaired, by specific endonucleases and exonucleases that are present. Presents the physical and biologic responses to ionizing radiation.[16]



Interaction of radiation in cell: Physical and biological response of ionizing radiation

Cells are more radiosensitive during the phase of cell division known as mitosis, when the chromatin material is being distributed to daughter cells. Hence rapidly dividing cells like intestinal epithelium, bone marrow cells, reproductive cells are more radio sensitive. Highly differentiated tissues like muscle and brain are least radiosensitive. Direct and indirect interactions of radiation with cell ultimately result in cell modifications like gene mutation, cell Tran's formation and chromosome alteration and cell death

EFFECT OF RADIATION ON HUMAN BODY

The harmful effects of radiation in human body are classified as
(i) Somatic effects and
(ii) Genetic effects.

The radiation effects, arises due to the damage Somatic cells are called somatic effects. It is produced in an exposed individual during his lifetime. The magnitude of the somatic effects vary with the nature of exposure (whole body or partial exposure). The hereditary effects are due to damage to reproductive cells and manifest in the progeny of the exposed person.[17]

EARLY SOMATIC EFFECTS (WHOLE BODY IRRADIATION)

Somatic effects may appear immediately after exposure, within a few hours to weeks or much later (after years - decades). The early effects are due to an acute exposure (large doses over a short period of time) and attributed to depletion of cell population due to cell death. The amount of radiation damage depends on the rate at which the radiation is delivered. High dose delivered in a short time may result in severe damages to tissues. The same dose delivered over several months allows the repair mechanisms to function fully. Hence, somatic effects listed in the table may not manifest, if the person receives the dose over aprolonged period.

EARLY SOMATIC EFFECTS (PARTIAL BODY IRRADIATION)

Partial body exposure to the above dose ranges produces only local effects. A whole body exposure to a dose of 4 Gy can be lethal. But exposure of a part of the body to the dose will not be life threatening. However, it can produce certain serious local effects. The seriousness of the local effects too depends on the dose rate and the period of exposure etc. All the early somatic effects do have a threshold dose, below which they do not occur. Beyond the threshold dose, severity of the effect increases with the dose. Since the threshold doses are much higher than the normal occupational dose, these effects may not occur from normal occupational exposure to radiation.[18]

LATE SOMATIC EFFECTS

Exposure to low levels of radiation over a prolonged period, may lead to late effects. Persons who recover from early somatic effects too may develop late somatic effects in life. Late effects are characterized by a latent period, which can be as long as 30 years. The important late effects are cataract and cancer. Dose needed to produce cataract may be greater than 8 Gy of fractionated irradiation (not acute) with low LET radiation and the latent period may be 5-10 years. The biological process required to transform the damaged cells to a cancer cell is very complex and the latent period may vary from 2-5 years for leukemia (blood cancer) and 5-30 years or more in the case of cancers of the lung, bone etc.

HEREDITARYEFFECTS

Hereditary effects occur in the progeny of exposed individuals when reproductive cells carrying radiation-induced damages(mutations)participate in the process of fertilization. Only that amount of radiation dose to reproductive organs, which occurs up to the time of conception, can affect the general characteristics of the off spring. However, the present knowledge on hereditary effects is limited to laboratory animals. No evidence for increase in hereditary effects was observed in human population exposed to both high and low dose of radiation. Hereditary And both early and late somatic effects of radiation can be classified into two categories, namely (i) deterministic effects and(ii)stochastic effects.

DETERMINISTIC EFFECT

A deterministic effect (non-stochastic) is one "which increases in severity with increasing absorbed dose in affected individuals' '. It results in cell killing due to degenerative changes in the

exposed tissues. It may appear at higher doses (> 0.5 Gy) and soon after the dose is received. It have thres hold dose, below which the effect is not seen. All somatic effects except cancer, as mentioned above are deterministic effects of radiation. All these effects will definitely appear in the exposed individual, if the radiation dose received is above the respective threshold doses. Examples are skin erythema, epilation, organ atrophy, fibrosis, cataract, blood changes, and reduction in sperm count. [19]

STOCHASTIC EFFECT

Astochasticeffectisoneinwhich"theprobabilityofoccurrenceincreaseswithincreasingabsorbeddoserathanitsseverity". It is very important at very low levels (< 0.5 Gy). Any dose, however small, is effective for a certain level of risk for induction of stochastic effects. The risk increases as the dose increases. It have no thres hold dose and the chance of occurrence increases with dose and independent of sex and age. Stochastic effects are the principle health risk from low level radiation, which is like lying diagnostic radiology and Nuclear medicine. Radiation induced cancer and genetic effects are examples for stochastic effects. Hence the risk of stochastic effects cannot be completely avoided. However, it can be minimized to an acceptable level[l]

Radiation Induced Cancer

Radiationinducedcancersmayappearonlysomeyearsaftertheradiationwasreceived.Thisisknownaslatentperiod,whichmayextendfrom10to30 years. The risk of inducing a particular type of cancer is measured by comparing the number of cancers produced in the irradiated population sample in excess of those expected in the same size of unirradiated population sample. This is known as Risk factor for the particular cancer. Leukemia has the highest risk Factor among all cancers, since tissue cells are rapidly dividing.

Genetic effects are caused by radiation induced damage to the genes or chromosomes in the ova or spermatozoa. The above damage is due to ionization and subsequent faulty recombination of the molecules which make up the chromosomes. As a result the biological code contained by the genes on the chromo somes gets altered and produce structure a lab normality in the chromo some. It will be passed on to the future generations if reproduction takes place. Severe genetic effects are not observed due to the short life span of the individual and inability to reproduce. Only less severe effects are seen in the human population as a result of reproduction. Epidemiological Studies Carried out on 30,000 children born to the survivors of atom bomb (500mSv) do not show an increase in the incidence of genetic dis orders. There is no direct evidence of either elevated cancer risks or genetic disorders among human population exposed to low level radiation.

To protect the future generations, minimize the use of artificial radiations and adopt protection devices such as gonad shield in children, during radiography. (Fig. A), summarizes both early and late biologic effects dueto radiation exposure from 0.001mSvto20Sv.

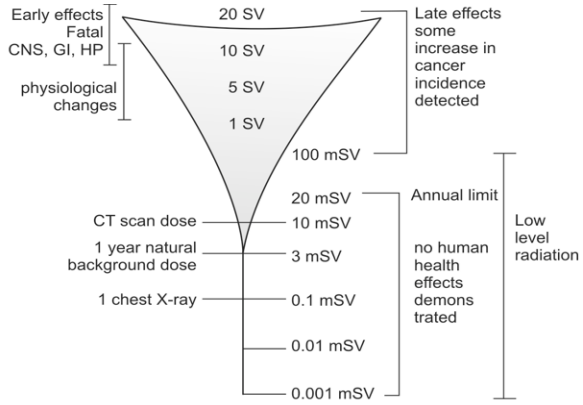


Fig. A: The early and late biologic effects of radiation withdoserangingfrom0.001mSvto20SV

RADIATION EFFECTS ON DNA

The ionizing radiation deposits energy in the DNA molecule and produces chemical changes, which leads to structural changes. This includes (i) hydrogen bond breakage, (ii) molecular dehydration, and (iii) intermolecular and intramolecular cross linking. The rupture of hydrogen bonds, which link the DNA base pairs, may result in irreversible structural changes in the molecule. DNA molecular breakage may occur as single strand breaks, double strand breaks, base loss or base changes occurring in DNA. Single strand breakage between the sugar and the phosphate can rejoin. Oxygen can cause the broken strand to become peroxidized, and prevent it from rejoining. Thus the presence of oxygen potentiates the radiation damage.

A double strand break are genotoxic lesions that can result in chromosome aberrations. This may lead to carcinogenesis through activation of oncogenes, inactivation of tumor suppressor genes, or loss of heterozygosity. Single strand breaks are easily repairable than double strand breaks as far as the low LET radiation is concerned (Fig. B).

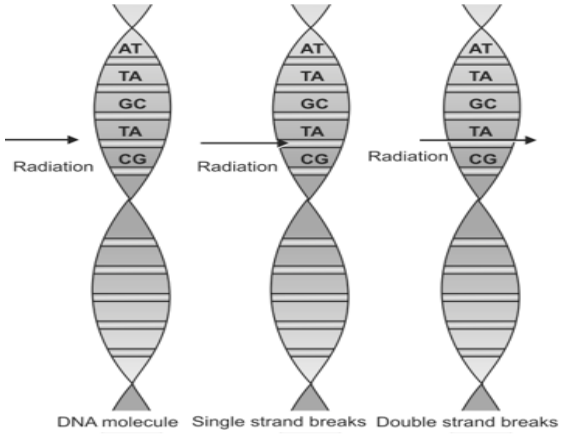


Fig. B: Radiation action on DNA molecule: Single and doubles trand breaks

Molecular cross linking is another common structural change, as resul to fre active sites at the poin to chain breakage. Cross linking may be between two DNA molecules, DNA and aprotein, two base pairs with in DNA.

Chromosome breaks produced by radiation do occur and can be observed microscopically. Chromosomal damage that occurs before DNA replication is called chromosome aberrations, whereas that which occurs after DNA synthesis is called chromatid aberrations. In the latter, only the daughter of one of the damaged chromatids pairs is affected. Repair of chromosomal aberrations depends on stage of the cell cycle, and type and location of the lesion. There is a strong force of cohesion between broken ends, resulting in rings and di centric formation. Chromosomal aberrations in human lymphocytes can be scored and used as a biological dosimeter to estimate radiation dose. For this lymphocytes are cultured from human blood samples. It is stimulated to divide, allowing karyotype to be performed. The cells are arrested at metaphase, and the frequency of rings and di-centric are scored. Total body doses > 0.25 Gy can be estimated in the above method.

Genetic Risk

Genetic risk is the result of radiation exposure to the gonads. Genetic risk analysis assumes that the (i) exposed population consists of all ages and both sexes and (ii) severe genetic effects in the next two generations. The genetically significant dose (GSD) is an index to estimate the radiation induced mutation in germ cells of a given population. The sensitivity of a population to radiation induced damage is measured by doubling dose. It is defined as the dose required per generation to double spontaneous mutation rate. The spontaneous mutation rate is about 5 × 10-6 per locus and 15 × 10-4 per gamete for chromosome abnormalities. The doubling dose for humans is estimated as ~1Gy per generation, which is extrapolated from animal data.A dose 100 mGy would produce only about 200 additional genetic disorders per 1 million live births (0.02 % per 100 mGy) in the first generation, whereas the normal incidence is about 1 in 20 (5%). Hence the 100 mGy dose can cause additional genetic disorders of about0.4% {(5.02-5)/5) × 100} only. The usual diagnostic and occupational exposures would not be expected to result in any significant genetic risk to their progeny.[20]

How x ray Damage to DNA

X-rays are a type of ionizing radiation that can cause damage to DNA through several mechanisms. The primary mechanism is the creation of free radicals, which are highly reactive molecules that can damage DNA and other cellular components. X-rays can also directly break the bonds in DNA, leading to breaks or cross-links in the DNA strands. When free radicals are created by x-ray exposure, they can react with the DNA molecules in a cell, causing oxidative damage to the DNA. This can result in the formation of various types of DNA lesions, including single-strand breaks, double-strand breaks, and base modifications. If these lesions are not repaired, they can lead to mutations in the DNA sequence, which can have a range of harmful effects on the cell, including increased risk of cancer. X-rays can also directly break the bonds in the DNA backbone, leading to strand breaks or cross-links between the strands. These types of DNA damage can also result in mutations, as well as other harmful effects on the cell, such as apoptosis (programmed cell death).

The severity of the DNA damage caused by x-rays depends on several factors, including the intensity and duration of the exposure, the type of tissue being exposed, and the individual's overall health and susceptibility to radiation damage. To repair DNA damage caused by x-ray exposure, cells have several mechanisms, including base excision repair, nucleotide excision repair, and homologous recombination. These mechanisms work to detect and repair DNA damage, replacing any missing or damaged nucleotides with new ones. However, if the amount of damage is too extensive, or if the repair mechanisms are overwhelmed, the cell may undergo programmed cell death or become cancerous, leading to a range of health problems and potentially life-threatening conditions. In summary, x-rays can cause damage to DNA through the creation of free radicals and direct breaks in the DNA backbone. This damage can lead to mutations and other harmful effects on the cell,

which can result in a range of health problems. However, cells have several mechanisms for repairing DNA damage caused by x-ray exposure, which can help to mitigate the harmful effects of radiation.

TREATMENT

The treatment of DNA damage caused by x-ray exposure depends on the extent and type of damage. In cases of mild damage, the cell's natural DNA repair mechanisms may be able to repair the damage without intervention. However, in cases of more severe damage, medical intervention may be necessary.

For example, in cases of x-ray-induced cancer, treatment may involve chemotherapy, radiation therapy, or surgery to remove the affected tissue. These treatments aim to kill or remove cancer cells and prevent the cancer from spreading to other parts of the body. In cases of x-ray-induced mutations, there is no specific treatment available to reverse the mutation. However, lifestyle changes such as avoiding exposure to other sources of radiation, eating a healthy diet, and getting regular exercise can help reduce the risk of further mutations and other health problems. Additionally, researchers are exploring various approaches to mitigate the effects of x-ray exposure on DNA, such as using antioxidants to neutralize free radicals or developing drugs that can enhance the cell's natural DNA repair mechanisms. In general, the best approach to treating x-ray-induced DNA damage is to prevent it from occurring in the first place. This can be done by minimizing unnecessary exposure to radiation, using appropriate protective equipment, and following recommended radiation safety guidelines in medical and occupational settings. In addition to the treatment options mentioned earlier, there are other strategies that can be used to mitigate the effects of x-ray exposure on DNA. One approach is to use radio protective agents, which are compounds that can reduce the damage caused by ionizing radiation. These agents work by scavenging free radicals or enhancing DNA repair mechanisms, and they have been shown to reduce DNA damage and other harmful effects of radiation in animal studies. However, their effectiveness in humans is still being studied, and more research is needed to determine their safety and efficacy.

Another approach is to use low-dose radiation therapy, which involves using very low levels of radiation to stimulate the body's natural repair mechanisms and reduce the risk of radiation-induced mutations. This approach has been shown to be effective in some cases, such as in the treatment of cancer, but more research is needed to fully understand its potential benefits and risks.

It is also important to note that prevention is the most effective strategy for minimizing the harmful effects of x-ray exposure on DNA. This can be achieved through appropriate radiation safety measures, such as using protective equipment and following recommended safety guidelines in medical and occupational settings. Additionally, individuals can take steps to reduce their exposure to radiation from other sources, such as by limiting their use of personal electronic devices that emit radiation. In summary, while there are various strategies for mitigating the effects of x-ray exposure on DNA, the best approach is to prevent unnecessary exposure in the first place. This can help to reduce the risk of DNA damage and other harmful effects of radiation exposure, and promote better overall health and well-being.

DISCUSSION

One of the major tools to treat tumors is the use of radio therapy. To improve the efficacy of radiation treatment there has been a significant interest in targeted new treatments for radio sensitization [5,7]. One of the most exciting aims for future therapies is to radiosensitive cells during replication in S phase. To radiosensitizer cells in S phase may be extremely promising because in this cell cycle phase cells are normally highly resistant to ionizing irradiation. The mechanism guarding against radiosensitivity is the DNA damage response (DDR), a signaling network involving multiple pathways including checkpoint activation and DNA repair [1,16].

When activated during S phase, these distinct as well as overlapping and/or cooperating checkpoint pathways delay S phase progression. This delay allows the cell to coordinate the multiple DNA repair systems active during S phase, like base excision-, nucleotide excision-, mismatch-, and DSB repair [4,33]. The intra-S checkpoint modulates the rate of DNA synthesis by influencing a number of parameters: the overall number of active origins, the chronological program of origin firing, the rates of movement of all active forks, and the occurrence of fork stalling events. To date it is not fully understood how these processes are affected by different types of DNA damage, either as a direct physical result of DNA lesions or via the action of the checkpoint. The activation of the intra S phase checkpoint occurs via recognition of the DNA damage by the sensor multi protein complexes MRN (Mre11-Rad50-Nbs1) for ATM (Ataxia telangiectasia mutated) or

by Rad17/9-1-1 complex (Rad17, Rad9-Rad1-Hus1) for ATR (Ataxia telangiectasia and Rad3 related). ATM and ATR themselves transduce signals to the effector checkpoint kinases Chk1 and Chk2. ATM primarily activates Chk2 and ATR activates Chk1, although considerable crosstalk between both pathways exists [12].

Ionizing irradiation induces several types of DNA lesions, base damage (BD), single strand breaks (SSB), double strand breaks(DSB), and DNA interest and cross links (ICL). Of these, DSB are expected to be the most toxic, but because of their low number after irradiation their importance at replication forks could be overestimated compared to others, like SSB and BD, which are produced with considerably higher yields. When cells enter S phase in presence of one or several of these types of damage, each of them have the potential to be converted to secondary DSB. A secondary DSB represents a special risk for the cell because recognition by the DDR response network might differ from primary DSB and has therefore a high potential to be mutagenic when repaired by error-prone mechanisms.

Ionizing irradiation induces all the types of DNA damage mentioned, and for cells synchronized in early S phase a transient block of origin firing was observed after irradiation [21]. However, to date it is not understood which types of lesions caused by irradiation are most detrimental to replication. To get more insight, the effect of ionizing irradiation, BD, SSB, DSB, and ICL on Chk1 phosphorylation, on replication initiation, elongation, and fork stalling as well as cell cycle progression was measured [22-23].

CONCLUSION

X-rays can cause significant damage to DNA, which can have harmful effects on the cell and increase the risk of cancer. Understanding the mechanisms underlying X-ray-induced DNA damage and repair is essential for developing effective strategies for protecting patients from harmful effects.

The primary mechanism through which X-rays damage DNA is the generation of free radicals, which can cause oxidative damage to the DNA bases, sugars, and phosphates. This damage can result in various types of DNA lesions, including single-strand breaks, double-strand breaks, and base modifications. However, cells have several mechanisms for repairing DNA damage caused by X-ray exposure, including base excision repair, nucleotide excision repair, and homologous recombination.

Medical professionals carefully administer X-rays to minimize the risk of DNA damage and other harmful effects on the patient. One common strategy is to limit the amount of radiation exposure by using lead shields or other protective barriers. Another approach is to use imaging techniques that require less radiation, such as ultrasound or magnetic resonance imaging (MRI).

In cases where DNA damage has occurred due to X-ray exposure, treatment options depend on the extent and type of damage. Mild damage may be repaired through the body's natural repair mechanisms, while more severe damage may require medical intervention. Treatments can include medications that stimulate DNA repair processes or procedures that remove damaged cells.

Ongoing research continues to advance our understanding of the molecular mechanisms underlying X-ray-induced DNA damage and repair, with the ultimate goal of improving the safety and effectiveness of X-ray-based medical procedures. By developing new strategies for minimizing the risk of DNA damage and improving the body's natural repair mechanisms, researchers aim to make X-ray procedures safer and more effective for patients.

The **FUTURE DIRECTION** of radiation's harmful effects on DNA includes several areas of focus, such as:

1. Molecular mechanisms: Further research is needed to understand the molecular mechanisms underlying radiation-induced DNA damage and repair. This research could help identify novel targets for preventing or repairing DNA damage and improve our understanding of the long-term effects of radiation exposure.
2. Genetic factors: Research is needed to identify genetic factors that may increase an individual's susceptibility to radiation-induced DNA damage. This knowledge could help develop personalized treatment plans for patients undergoing radiation therapy or imaging procedures.
3. Radiation shielding: New materials and technologies for radiation shielding are being developed to minimize the risk of DNA damage and other harmful effects on patients. Research in this area is ongoing, with the goal of developing more effective and affordable shielding options for medical facilities.

4. Low-dose radiation: Research is needed to better understand the effects of low-dose radiation exposure on DNA and how to minimize the risk of harm while still achieving effective imaging or therapy. This area of research could lead to the development of more precise and targeted radiation therapies with fewer side effects.
5. Clinical applications: Future research will continue to explore the use of radiation therapy and imaging techniques for treating and diagnosing various diseases. This research will aim to improve the safety and effectiveness of these procedures while minimizing the risk of DNA damage and other harmful effects.

Overall, the future direction of research on radiation's harmful effects on DNA will continue to advance our understanding of the underlying mechanisms, identify novel strategies for prevention and repair, and improve the safety and effectiveness of radiation-based medical procedures.

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