HEALTH RISK AND BIOLOGICAL EFFECT OF CARDIAC USING IONIZING RADIATION IMAGING TECHNIQUES

BY

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A PROJECT SUBMITTED TO THE SCHOOL OF POSTGRADUATE STUDIES, NASARAWA STATE UNIVERSITY KEFFI, IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF A POSTGRADUATE DIPLOMA IN MEDICAL AND RADIATION PHYSICS

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DECLARATION

I hereby declare that the work in this project has been written by me and it is a report of my research work. It has not been presented in any previous application for postgraduate diploma (PGD) or degree. All quotations are indicate and sources of information specifically acknowledged by means of references.

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CERTIFICATION

The projcet title “Health risk and biological effects of cardiac using ionizing radiation imaging techniques” meets the regulations governing the award of postgraduate diploma in radiation and medical physics school of postgraduate studies, NasarawaState university, Keffi, and is approved for its contribution to knowledge.

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DEDICATION

I dedicate this project work to Almighty God for his protection and guidance throughout the course of my study.

ACKNOWLEDGEMENT

I thank the Almighty God creator of heaven and earth for his mercy, guidance, love and grace toward me. My profound gratitude goes to my project supervisor Dr. Umar Ibrahim for his useful comment, guidance, words of encouragement and materials surrendered for the success of this project, which made it possible for me to complete this research work successfully. Indeed I thank God for you sir.

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Dear mother Late Mrs. Elizabeth EneyiOtegwaOdey I cannot quantify my thanks for you, indeed you are too much. May God beautify your seeds with excellence and satisfaction

My appreciation goes to Larai Osuza for your concern and support to see that I am successful during my programme. And to all my friends for their prayers, encouragement and nice support God bless you all.

ABSTRACT

Cardiac diagnostic or therapeutic testing is essential tool for diagnosis and treatment of cardiovascular disease, but it also involves considerable exposure to ionizing radiation. Every exposure produces a corresponding increase in cancer risk, and risks are highest for radiation exposure during infancy and adolescence. Recent studies on chromosomal biomarker corroborate the current radioprotection assumption showing that even modest radiation load due to cardiac catheter-based fluoroscopic procedures can damage the DNA of a cell. It was reviewed in the project the biological and clinical risk of cardiac imaging employing ionizing radiation it was also discuss the perspective, offered by the use of molecular biomarkers in order to better assess the long-term development of health effect.

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CHAPTER ONE

INTRODUCTION

1.4 Background to the Study

The increasing exposure to medical radiation in western countries is a hot issue that the medical community needs to appreciate because it may likely result in an increase in the incidence of imaging related cancer in the future (Picano, 2004).

Medical use of radiation is the largest man made source of radiation exposure to the general population. According to the recent report on medical radiation received from clinical imaging has increased by 700% between 1980 and 2006 (Mettle, *et al.,* 2008).

The current annual collective dose of radiation exposure received by the U.S population has been calculated as roughly equivalent to the total worldwide collective dose generated by the nuclear catastrophe at chemobyl (Amis *et al.,* 2007).

Many cardiac diagnostic or therapeutic testing, such as cardiac scans accounting for 750% of all imaging examinations, involve considerable exposure to ionizing radiation (Gerber *et al.*, 2009).

A contemporary cardiac patient is exposed to a significant cumulative effective dose (a median cumulative effective dose of 60 mSv per head) from multiple tests, often repeated needlessly (Bedetti *et al.,* 2008).

Three central principle provide the foundation for radiation protection 1 justification (the benefit of radiation exposure outweighs any accompanying risk) 2 optimization (total

exposure remain as low as reasonably achievable, ALARA principle) 3 dose limits (dose limits are applied in order to ensure that no one is exposed to unacceptably high risk).

In cardiological practice, therefore every effort should be done to justify the indication and to optimize the dose during ionizing testing. The imaging examination should conferarelevant clinical information on patient management, i.e the benefit deriving from the examination must be greater than the long-term risk associated with the exposure (Hampton, 2006).

The evaluation of the health effects of low dose ionizing radiation has always been the main issue in radiological protection. In this project, we review the biological and clinical risks of diagnostic imaging employing ionizing radiation as well as to discuss the perspectives offered by the use of surrogated molecular biomarkers in order to better assess the long-term development of health effects.

1.2 Statement of Problem

Many cardiac diagnostic or therapeutic testing such as cardiac catheterization, Computed Tomography (CT) and nuclear medicine scans, accounting for 750% of all imaging examinations involve considerable exposure to ionizing radiation. A contemporary cardiac patient is exposed to a significant cumulative effective dose (a median cumulative effect dose of 60 mSv per head) form multiple tests often repeated needlessly.

1.3 Aim of the Study

The aim of this project is to investigate the risk and effect of cardiac ionizing radiation form epidemiology to genes:

1.4 Objectives of the Study

The objectives of this research work are to;

i. Review the clinical risk of medical ionizing radiation exposure

ii. Review radiation risk at regular interval progress worldwide in order to reach a balanced view of the risk involved.

iii. Review the epidemiological studies of human populations, including atomic bomb survivors, patient exposed to radiation form diagnostic and therapeutic medical studies, as well as studies form occupational exposures and form exposure due to releases of radioactive material into the environment.

iv. Review cumulative exposure of dose in multiples of dose from a simple chest x-ray and corroding cancer risk.

1.5 Significance of the Study

The project is intended to provide an insight to what exist in the body system or cardiac when in contact with ionizing radiation imaging form epidemiology to gene and dose limits are applied in order rot ensure that no one is exposed to an unacceptably high risk.

1.6 Scope of the Study

Risks to patients posed by exposure to medical radiation. The biological consequences of ionizing radiation fall into two categories.

Deterministic effects such as skin erythema, epilation, or contract formation predictably occur at certain thresholds of absorbed dose to a specific tissue. The hypothefical complication of diagnostic medical radiation exposure that is of greatest concern, the risk

of inducing malignancies, is a stochastic, or random, effect in which the interaction of radiation with cellular molecules may cause damage sufficient that a malignancy may result later.

CHAPTER TWO

LITERATURE REVIEW

2.1 Radiation

Radiation is a process in which energetic particles or energetic waves travel through a vacuum, or through matter containing media that are not required for the propagation. Wave of mass filled medium itself, such as water wave or sound wave are usually not considered to be forms of radiation in this sense.

Everyone is exposed to radiation on a daily basis primarily from naturally occurring cosmic rays, radioactivity in soil and radioactive element incorporated in the body, man-made sources of radiation such as x-rays or fallouts form historical nuclear weapon testing also contribute, but to a less extent about 80% of background radiation originated from naturally occurring sources with the remaining 20% resulting from man-made source. Radiation refers to the propagation of waves and particles through space and includes both electromagnetic radiations, atomic and sub-atomic, particle radiation; electromagnetic radiation has a broad continuous spectrum of energy that includes visible light, radio waves etc.

All electromagnetic radiations travel at the speed of light, particles radiation include alpha particles, beta particles, neutrons, protons, and heavy ions. The speed and energy of particles radiation depend on the sources of the radiation and any other subsequent interaction of the particles with other matter.

The uses of radiation include smoke detectors, treatment of cancer, sterilizing medical equipment etc (Onoja, 2004).

2.2 Classes of Radiation

Radiation is classified into two, ionizing and non-ionizing radiation, according to whether it ionizes or does not ionize ordinary chemical matter.

The word radiation is often colloquially used in reference to ionizing radiation (example gamma ray, x-rays) but the term radiation may correctly also refer to non-ionizing radiation (example radio weaves, heat or visible light) as well. The particles or waves radiate (i.e travel outward in all directions) from a source.

This aspect leads to a system of measurement and physical unit that are applicable to all types of radiation, because radiation expands as it passes through space and its energy is conserve (in vacuum), the power of all type of radiation follow an inverse square law in relation to the distance from the source.

2.2.1 Ionizing Radiation

Radiation that falls within the "ionizing radiation" range has enough energy to remove tightly bound electrons from atoms, thus creating ions. This is the types of radiation that people usually think of as 'radiation'. We take advantage of its properties to generate electric power, to kill cancer cells, and in many manufacturing processes.

The energy of radiation shown on the spectrum of fig. 2.1 increases from left to right as the frequency rises.

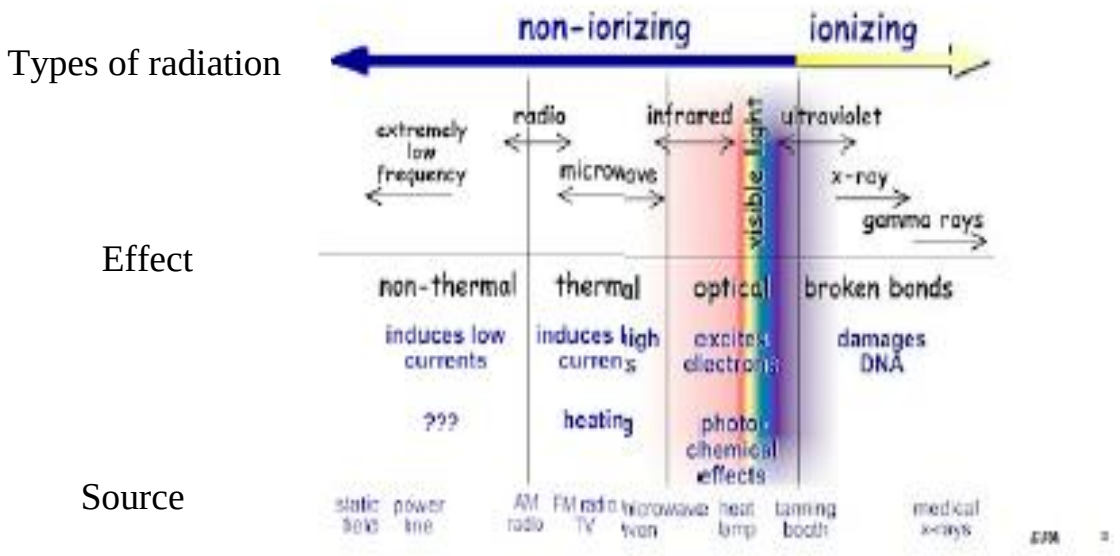


Fig. 2.1 types of radiation in the electromagnetic spectrum (Markos *et al.*, 1999).

Higher frequency ultraviolet radiation begins to have enough energy to break chemical bonds. X-ray and gamma ray radiation, which are at the upper end of electro-magnetic radiation, have very high frequencies (in the range of 100 billion hertz) and very short wavelengths of about 1 picometer (1 trillion of meter). Radiation this range has extremely high energy. It has enough energy to strip off electrons or in the case of very high-energy radiation, break up the nucleus of atoms.

Each ionization releases approximately 33 electron volts (eV) of energy. Material surrounding the atom absorbs the energy. Compared to other types of radiation hat may be absorbed, ionizing radiation deposits a large amount of energy into a small area. In fact, the 33ev form one ionization is more than enough energy to disrupt the chemical bond between two carbon atoms.

All ionizing radiation is capable, directly or indirectly, of removing electrons form most molecules.

2.2.2 Non-Ionizing Radiation

Radiation that has enough energy to move around atoms in molecule or cause them to vibrate, but not enough to remove electrons, is referred to as “non-ionizing radiation.” Examples of this kind of radiation include visible light and microwaves. We take advantage of the properties of non-ionizing radiation for common tasks.

i. Microwave radiation telecommunications and heating food.

ii. Infrared radiation infrared lamps to keep food warm in restaurants

iii. Radio waves broadcasting.

Non-ionizing radiation ranges from extremely low frequency radiations, shown on the far left through the audible, microwave, and visible portions of the spectrum into the ultraviolet range.

Extremely low-frequency radiation has very long wavelengths (on the order of a million meters or more) and frequencies in the range of 100 hertz (cycles per second) or less. Radio frequencies have wavelengths of between one and 100 meters and frequencies in the range of one million to 100 million hertz. Microwaves that we use to heat food have wavelengths that are about one hundredth of a meter and have frequencies of about 2.5 billion hertz.

Both ionizing and non-ionizing radiation can be harmful to organisms and can result to changes to the natural environment in general; however ionizing radiation is far more harmful to living organism per unit of energy deposited than non-ionizing radiation since the ions that are produce event at low radiant power has the potential to cause DNA damage.

Non-ionizing radiation is usually considered to have a safe lower unit, especially as thermal radiation, also radiation refers to the particles or energy released during radioactive decay. The radiation emitted maybe in the form of particles such as neutrons, alpha particle and beta particles or waves of pure energy such as gamma and x- rays (ICRP, 2008).

2.2.3 Types of Radiation

The radiation one typically encounters is one of four types: alpha radiation, beta radiation, gamma radiation and x-radiation. Neutron radiation is also encountered in

nuclear power plant and high altitude flight and emitted from some industrial radioactive sources.

2.2.4 Radiation Dose

Sunlight feels warm because our body absorbs the infrared rays it contains. But, infrared rays do not produce ionization in body tissue. In contrast ionizing radiation can impair the normal functioning of the cells or even kill them. The amount of energy necessary to cause significant biological effects through ionization is so small that our bodies cannot feel this energy as in the case of infrared rays, which produce heat (Hampton *et al.*, 2010).

The biological effects of ionizing radiation vary with the types and energy. A measure of the risk of biological harm is the dose of radiation that the tissues receive. The unit of absorbed radiation dose is the sievert (Sv). Since one sievert is a large quantity, radiation doses normally encountered are expressed in millisievert (mSv) or microsievert (uSv) which are one thousandth and one millionth of a sievert respectively. For example, one chest x-ray will give about 0.2 mSv of radiation dose.

On average, or radiation exposure due to all natural background sources amountas to about 2.4 mSv a year, though this figure can vary, depending on the geographicallocation, by several hundred percent (Ajayi *et al.*, 2009).

In homes and building, there are radioactive elements in the air. These radioactive elements are Radon (radon- 222) thorium (Radon-220) and by products formed by the decay of radium 226) and thorium present in may sorts of rocks, other building materials and in the soil. By far the largest sources of natural radiation exposure comes from

varying amounts of uranium and thorium in the in the soil sound the world. The radiation exposure due to cosmic rays is very dependent on attitude, and slightly on latitude. People, who travel by air, thereby increase their exposure to radiation (Chukwuocha *et al.*, 2010).

2.2.5 Radiation Interaction with Matter

The interaction of radiation with matter depend on the type of radiation; each type of radiation has its separate way of interacting with matter as the interact has to do with the quantum energy of each o radiation (Glenn, 2010). Here are the types of radiation and their mode of interaction with matter.

2.2.6 Microwave Interactions

The quantum energy of microwave photons is in the 0.00001 to 0.001ev which is in the range of energies separating the quantum states, of molecular rotation and torsion. The interaction of microwaves with matter other than metallic conductors will be to rotate molecules and produce heat as result of that molecular motion. Conductors will strongly absorb microwaves and any lower frequencies because they will cause electric currents which will heat the material. Most matter, including the human body, is largely transparentto microwaves (Karatzis, 2008). High intensity microwaves, as in a microwave oven where they pass back and forth through the food millions of times, will heat the material by producing molecular rotations and torsion. Since the quantum energies are a million times lower than those of x-rays, they cannot produce ionization and the characteristic type of radiation damage associated with ionizing radiation.

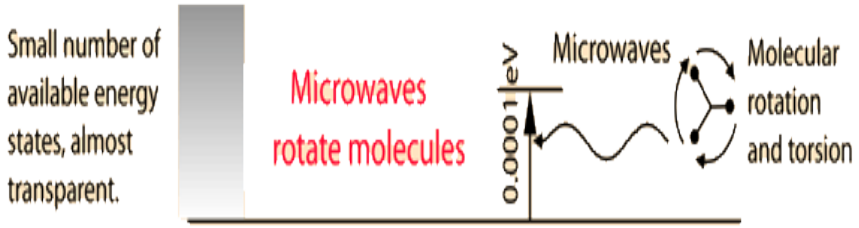


Fig. 2.2 Microwaves Interaction with Matter (Nave, 2017).

2.27. Infrared Interaction

The quantum, energy of infrared photons is in range 0.001 to 1.7ev which is in the range of energies separating the quantum states of molecular vibrations. Infrared is absorbed more strongly than microwaves, but less strongly than visible light. The result of infrared absorption is heating of the tissue since it increases molecular vibrational activity. Infrared radiation does penetrate imaging of subcutaneous blood vessel.

2.2.8 Visible Light Interactions

The primary mechanism for the absorption of visible light photons is the elevation of electrons to higher energy levels. There are many available states, so visible light is absorbed strongly. With a strongly light source, red light can be transmitted through the hand or a fold of skin, showing that the red end of the spectrum is not absorbed as strongly as the violet end.

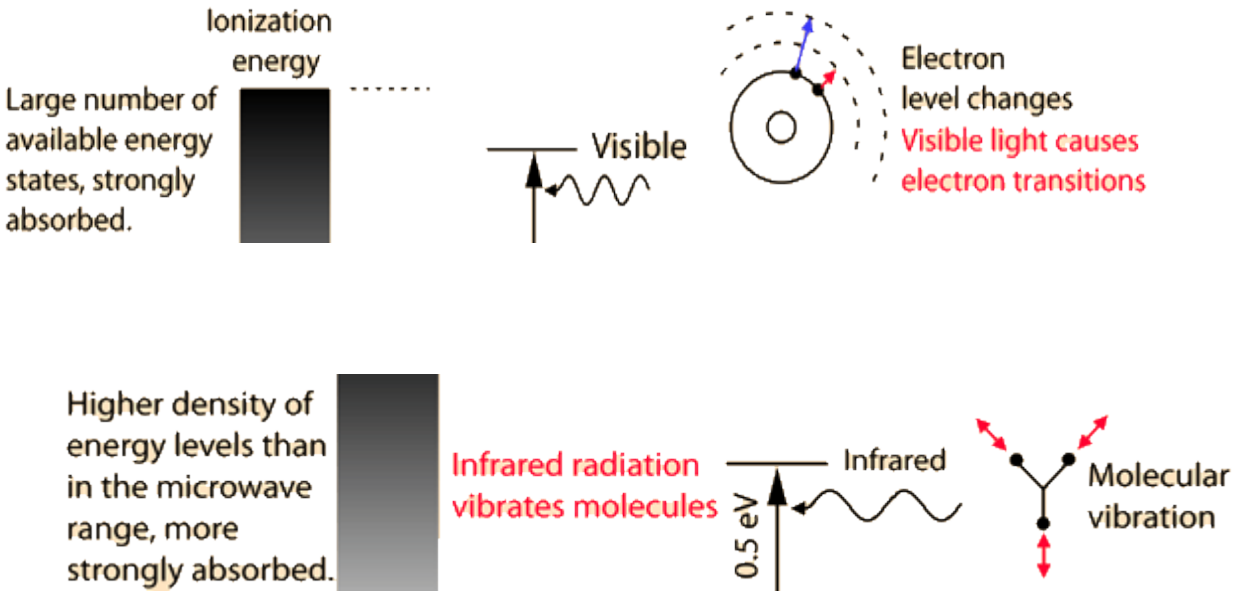


Fig. 2.3 visible light interaction with matter (Nave, 2017).

While exposure to visible light causes heating, it does not cause ionization with its risk. You may be heated by the sun through a car windshield, but you will not be sunburned that is on effect of the higher frequency UV part of sunlight which is bloc by the glass of the windshield.

2.2.9 Ultraviolet Interacts

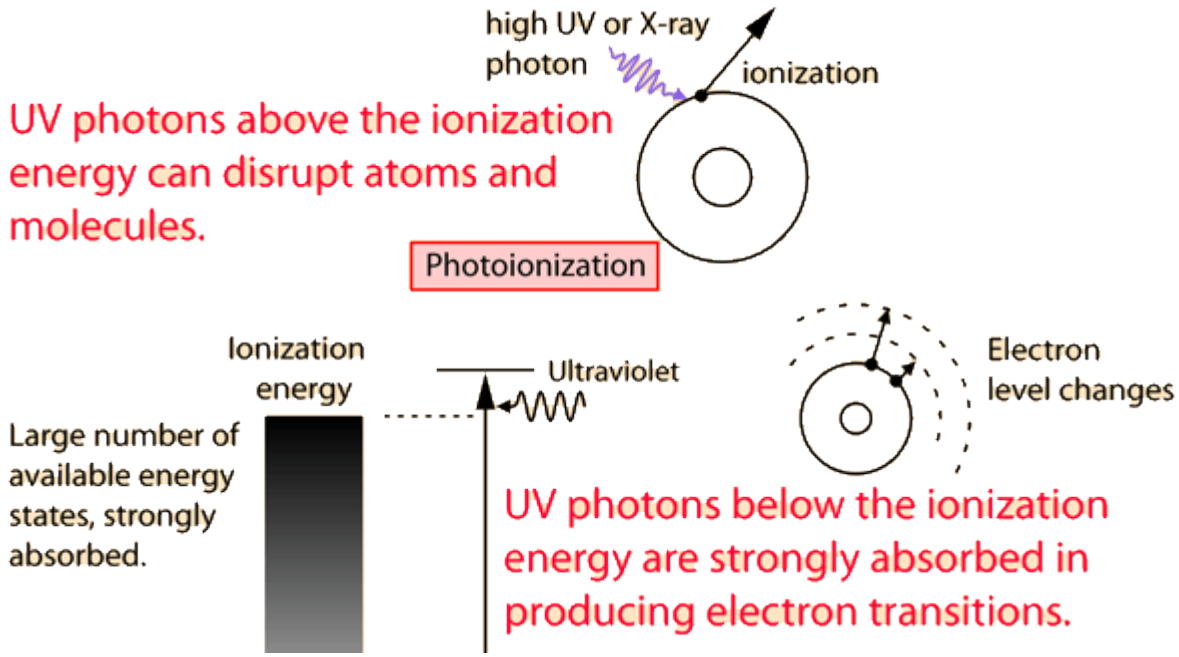


Fig.2.4Ultraviolet Ray Interact with matter (Nave, 2017).

The near ultraviolet is absorbed very strongly in the surface layer of the skin by electron transitions. As you got o higher energies, the ionization energies for many molecules are reached and the more dangerous photo ionization processes take place. Sunburn is primarily on effect of UV and ionization produces the risk of skin cancer.

The ozone layer in the upper atmosphere is important for human health because it absorbs most of the harmful ultraviolet radiation from the sun before it reaches the surface. The higher frequencies in the ultraviolet are ionizing radiation and can produce harmful

physiological effects ranging from sunburn to skin cancer. Health concerns for UV exposure are mostly for the range 290-330nm in wavelength, the range called UVB.

According to (Scotto, 2001), the most effective biological wavelength for producing skin burns is 29nm. Their research indicates that the biological effects increase logarithmical with the UVB range, with nm being only 0.1% as effective as 297nm for biological effects. So it is clearly important to control exposure to UVB (Mettler, 2008).

2.2.10 X-Ray Interaction

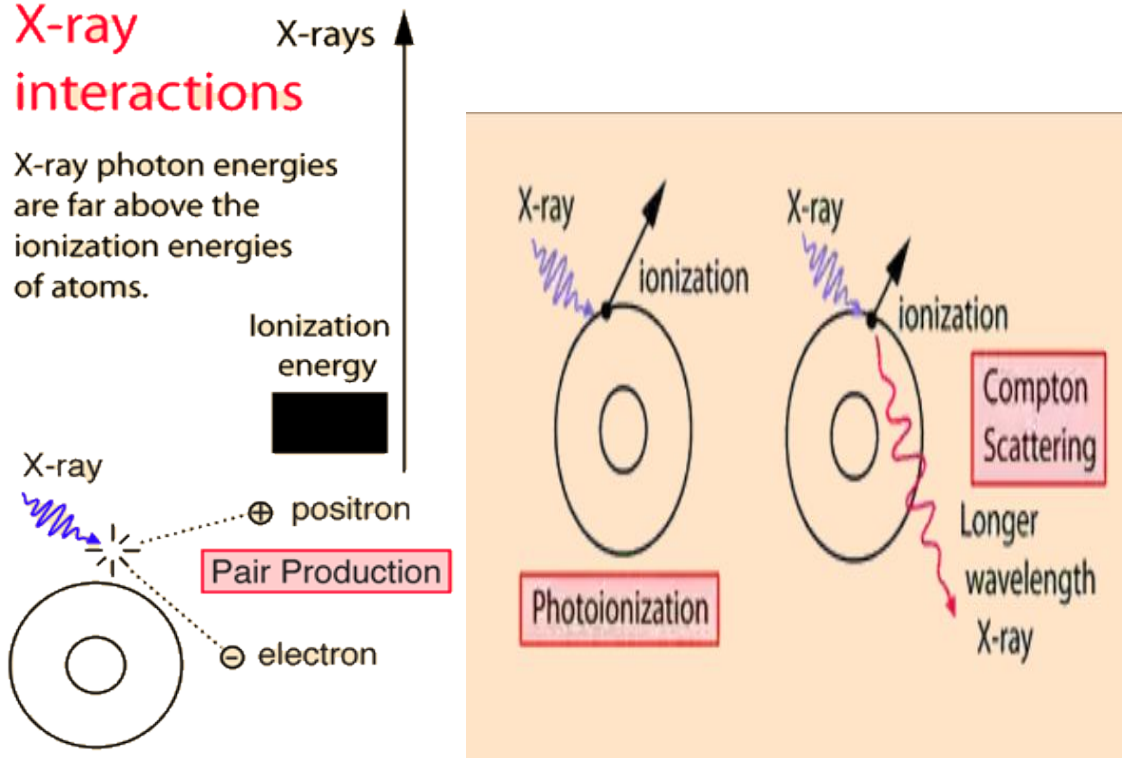


Fig. 2.5 x-Ray Interaction with Matter (Nave, 2017).

Since the quantum energies of x-ray photons are much too high to be absorbed in electron transitions between states for most atoms, they can interact with on electron only by knocking it completely out of the atom. That is all x-ray are classified as ionizing radiation. This can occur by giving all of the energy to an electron (photo ionization) or by giving part of the energy to the electron and the remainder to a lower energy photon (Compton scattering).

At sufficiently high energies, the x-ray photon can create an electron position pair.

2.3 Dose Limit

Everyone, everywhere, is exposed to radiation all the time. It is a natural part of the environment in which we live.

People are also exposed to man-made radiation predominantly in machine, but also from other sources. For some, radiation exposure is part of their work.

2.3.1 Terrestrial Radiation

Terrestrial radiation comes from the earth; everything is naturally radioactive, including rock, soil, water, air, animals, plants and food. The average dose form terrestrial radiation is 2 mSv per years. More than half of this is form radon in your home.

2.3.2 Cosmic Radiation

Cosmic radiation comes from the sun and outer space. The average dose form cosmic radiation is 0.4 mSvper year.

2.3.3 Medical Diagnosis

Medical procedures make up most of the man-made dose, by far. The average dose form medical diagnosis is 0.6mSV per year.

Some people are also exposed to radiation as part of their work; form industrial uses line nuclear power plants, from accidents, and even form left over's of atmospheric nuclear testing. On average, the dose from this is very small, about 0.01mSv per year.

These numbers are worldwide averages. Some people are exposed to less radiation, and some more. The table below includes typical ranges of annual dose.

Table 2.1 Annual average dose and ranges of individual doses of radiation by source (millisieverts[a])

Source or mode	Annual average dose (worldwide)	Typical range of individual dose	Comment
Natural source of exposure			
Inhalation (radon gas)	1.26	0.2-10	The dose is much higher in some dwellings
External terrestrial	0.48	0.3-1	The dose is higher in some locations
Ingestion	0.29	0.2-1	
Cosmic radiation	0.39	0.3-1	The dose increases with altitude.
Total natural	2.4	1-13	Sizeable population groups receive 10-20 millisieverts (mSv)

Table 2.2 Annual average dose and ranges of individual doses of radiation by source (millisieverts[a])

Source or mode	Annual average dose (worldwide)	Typical range of individual dose	Comment
Artificial source of exposure			
Medical diagnosis (not therapy	0.6	0-severa tens	The averages of different levels of health care range from 0.03 to 2.0mSv; averages for some countries are higher than that due to natural sources; individual doses depend on specific examinations.
Atmospheric nuclear testing	0.005	Some higher dose around test sites still occur	The average has fallen form a break of 0.11 mSv in 1963
Occupational exposure	0.005	~0-20	The average dose to all workers is 0.7 mSv most of the average dose and most high exposures are due to natural radiation (specifically radon in mines).
Chemobly accident	0.002[b]	In 1986, the average dose to more than 300.000 recovery workers was nearly 150	The average in the northern hemisphere has decreased from a maximum of 0.04 mSv in 1986. Thyroid dose were much higher.

		mSv, and more than 350,000other individuals received dose greater than 10 mSv	
Nuclear fuel cycle (public exposure)	0.002[b]	Doses are up to 0.02 mSv for critical groups at 1km form some nuclear reactor sites	
Total artificial	0.6	From essential zero to several tens.	Individual dose depend primarily on medical treatment occupational exposure and proximity to test or accident sites.

[a] Unit of measurement of effective dose

[b] Globally dispersed radionuclide's. The value for the nuclear fuel cycle represents the maximum per caput annual dose to the public in the future, assuming the practice continue for 100 years and derives mainly form globally dispersed, long-lived radionuclide's released during reprocessing of nuclear fuel and nuclear power plant operation (NUSCEAR, 2008).

Radiation dose is a measure of the amount of exposure to radiation. There three kinds of dose in radiological protection. Absorbed dose is a measureable, physical quantify, while equivalent dose and effective dose are specifically for radiological protection purposes.

Effective dose in particular is a central feature of radiological protection. It sums up any number of different exposures into a single number that reflects, in a general way, the overall risk. The concept may be complex, but it makes radiological protection practical to implement (ICRP, 2007).

2.3.4 Absorbed Dose

Absorbed dose is the amount of energy deposited by radiation in a mass. The mass can be anything water, rock, air, people, etc. absorbed dose is express in milliseverts (mGy).

2.3.5 Equivalent Dose

Equivalent dose is calculated for individual organs it is base on the absorbed too an organ, adjusted to account of the effectiveness of the type of radiation. Equivalent dose is expressed in millisieverts (mSv) to an organ.

2.3.6 Effective Dose

Effective dose is calculated for the whole body. It is sometimes called whole body dose.

It is the addition of equivalent doses to all organs, each adjusted to account for the sensitivity of the organ to radiation.

Effective dose is express in millisievertsmSv (ICRP, 2007).

2.4 Biological Effects of Ionizing Radiation

The biological effects of ionizing radiation are divided into two categories: deterministic and stochastic effects (Hall *et al.,* 2000).

2.4.1 Deterministic Effects

Such as erythema or cataract, have a threshold dose below which the biological response is not observed (table 2) some cardiological interventional procedures with long screening times and multiple image acquisition (e.g percutaneous coronary intervention, radio frequency ablation, etc) may give rise to deterministic effects in both staff and patients (Vano *et al.,* 2005).

2.4.2 A Stochastic Effect

A stochastic effect is probabilistic event and there is no known threshold dose (table 2).The likelihood of inducing the effect but not the severity, increases in relation to dose and may differ among individuals. Infact, the effect, of low dose of radiation less than 50 mSv do not cause on immediate problem to any body organ, but spread out over long periods of time after exposure (Tubiana *et al.,* 2006).

2.4.3 Damage to DNA

Which carries the genetic information in chromosomes in the cell nucleus, is considered to be the main initiating event by which radiation damage to cells result in development of cancer and hereditary discreas in the future children of exposed parents (ICRP, 2008).

Table 2.3 Biological effect of ionizing radiation (Vano, et al., 2005).

	Deterministic effects	**Stochastic effect**
Dose	Medium-high	Low
Occurhence time	Short	Long
Threshold	Yes	No
Cell biology	Cell death	DNA
Clinical effect	Skin lesions, erythema, ulcers, epilation, cataracts permanent sterility	Cancer, genetic effects

Ionizing radiation exposure produces long-term health risk through, both directly or indirectly (free radical interaction), damage to cellular DNA, producing oxidized bases, bulky DNA adducts strand breaks.

The cell has repair mechanisms against damage include by radiation as well as by chemical carcinogens. Consequently, biological effects of low dose radiation on living cells may result in three outcomes:

i. Injured or damaged cells repair themselves, resulting in no residual damages;

ii. Cells die; or

iii. Cells incorrectly repair themselves resulting in a biological change.

Therefore, the biological effects of stochastic effect are at DNA level and they may not be detected. The basic concept is that physical steps that lead o energy deposition and free radical formation occur with 10^{-5} to 10^{-6} seconds, whereas the biological expression of physical damage may occur a second or decades later (UNSCEAR, 2001).

2.4.4 Chemical and Biological Effects by Ionizing

On left side: From physical interaction (a few milliseconds) to clinical effects (decades later).

On the rights side: The corresponding molecular (DNA damage), cellular (cell damage or proliferation), and clinical events (such as cancer).

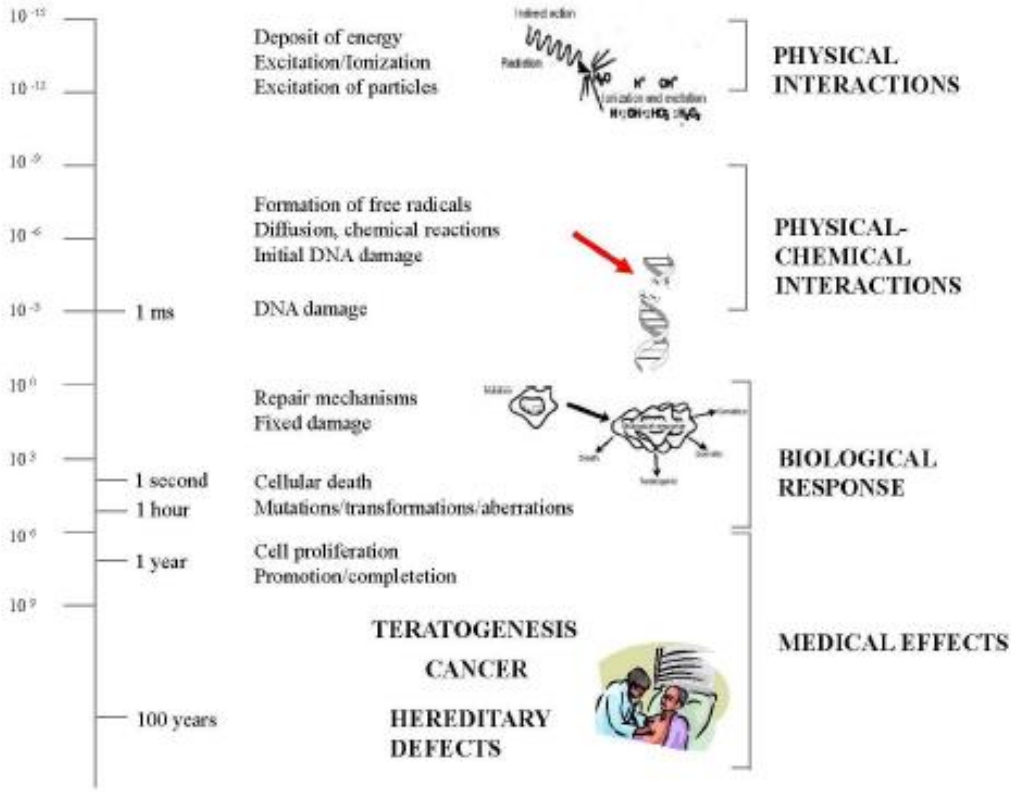


Fig. 2.6 chemical andbiological effects by ionizing radiation (UNSCEAR, 2001).

2.4.5 Radiation-Induced Mutation Contribute to the Multi Step Process of Human Cancer Arising from the accumulation of multiple genetic abnormalities (over-expression of genes, deletion of genes, or gene mutations), some of which must occur in critical genes that regulate proliferation and differentiation.

Genetic effects are the result of mutation produced in the reproductive cells of an exposed individual that are passed on to their offspring. These effects may show up as birth defects or other conditions in the future children of the exposed individual and succeeding generation.

Adverse hereditary effects that could be attributed to radiation have not been found, in epidemiological studies of children whose parents were exposed to radiation (BEIR, 2006).

However, studies conducted on mice and other organism have produced extensive data showing that radiation induced cell mutations in sperm and eggs can be passed on the offspring (BEIR, 2006).

Thus, there is no reason to believe that humans would be immune to this sort of harm (BIER, 2006)**.**

2.4.6 X-Rays

X-rays are a type of radiation called electromagnetic wave. X-ray imaging creates pictures of the inside of your body. The images show the parts of your body in different shades of black and white. This because different tissues absorb different amounts of

radiation. Calcium in bones absorbs x-rays the most, so bones look white. Fat and other soft tissues absorb less, and look gray. Air absorbs the least, so lungs look black.

The most familiar use of x-rays is checking for broken bones, but x-ray is also used in other ways. For example chest x-rays can spot pneumonia. Mammograms use x-rays to look for breast cancer

When you have an x-ray, you may wear a lead apron to protect certain parts of your body. The amount of radiation you get form on x-ray is small. For example, a chest x-ray gives out a radiation dose similar to the amount of radiation you are naturally exposed to from the environment over 10 days (NIH, 2016).

2.4.7 CT scan

CT scan, also known as computed tomography scan, makes use of computer-processed combinations of many measurements taken from different angles to produces cross sectional images (virtual "slices") of specific areas of a scanned object without cutting. Other terms include computed axial tomography (CAT scan) and computer aided tomography (NIH, 2016).

2.4.8 Fluoroscopy

Fluoroscopy is an imaging modality that uses x-ray to allow real-time visualization of body structures. During fluoroscopy, x-ray beams are continually emitted and captured on a screen, producing a real-time, dynamic image. This allows for dynamic assessment of anatomy and Function. High density contrast agents may be introduced into the patient to allow for greater differentiation between structures (WHO, 2018).

2.4.9 MRI

Magnetic resonance imaging (MRI) uses a large magnet and radio waves to look at organs and structures inside your body. Health care professionals use MRI scans to diagnose a variety of conditions, form turn ligaments to tumors. MRIs are very useful for examining the brain and spinal cord.

During the scan, you lie on a table that slides inside a funnel shaped machine. Doing the scan can take a long time, and you must stay still. The scan is painless. The MRI machine makes a lot of noise. The technician may offer you earplugs.

Before you get a scan, tell you doctor if you are:

i. Pregnant

ii. Have pieces of metal in your body you might have metal in your body if you have a shrapnel or bullet injury or if you are a welder.

iii. Have metal or electronic devices in your body such as a cardiac pacemaker or a metal artificial joint (NIH, 2016).

2.4.10 Nuclear Medicine

Nuclear medicine is a branch of medical imaging that uses small amounts of radioactive materials to diagnose and determine the severity of or treat a variety of diseases, including many types of cancer, heart disease, gastrointestinal, endocrine, neurological disorders and other abnormalities within the body.

Because nuclear medicine procedures are able to pinpoint molecular activity within the body, they offer the potential to identify disease in its earliest stages as well as a patient's immediate response to therapeutic interventions (Radiologyinfo, 2018).

2.4.11 Review of Related Work

Some work has been done on risk model CT scan in US Berrington *et al* (2009) the results estimated that approximately 29000(95%UL, 15000-45000) future cancers could be related to CT scans performed in the US in 2007. The largest contributions were form scans of the abdomen and Pelvis (n=14,000) (95%UL, 6900-25000), chest (n=4100) (95% UL, 1100-8700), as well as from chest CT angiography (n=2700) (95%UL, 1300-5000).

One third of the projected cancers were due to scans performed at the ages of 35 to 54 years compared with 15% due to scans performed at ages younger than 18 years, and 66% were in females Berrington *et al*.,(2009).

CHAPTER THREE

METHODOLOGY

3.1 Review of Clinical Risk of Medical Ionizing Radiation Exposure

Exposure carcinogenesis, teratogensis and heritable effects are the main health risk with ionizing radiation. Other non-cancer adverse effects especially atherosclerotic cardiovascular and cerebrovascular risk can occur following high dose radiation therapy, but more research is needed to fully asses these out comes at low and moderate dose (BEIR VII, 2006).

3.2 Review of Radiation Risk at Regular Interval Progress Worldwide in Order to Reach a Balanced View of the Risk Involved.

Radiation risk are reviewed at regular intervals by international and national radiological organizations by considering scientific progress worldwide in order to reach a balanced view of the risk involved.

The current consensus of these regulatory bodies is that for radiation protection purposes the most appropriate risk model at low doses is the so-called linear no-threshold (LNT) model, without threshold safe dose.

During last year'showever, two opposing concept to LNT model have emerged. In some have argued that risks are smaller than predicted by the linear no-threshold model Tubiana *et al., (*2006) or that low doses of radiation may even be beneficial because organisms posses the ability to respond to low-dose radiation by stimulating certain

protective functions (radiation adaptive response), including antioxidative capacity, DNA repair functions, apoptosis (Feinendegen, 2005).

Some postulate that low doses radiation are more harmful than previously thought because damage occurs not to the cell that was exposed to radiation but also to surround cells (Bystander effects) Azzam *et al.*, (2004).

The most recent update of the health risk of exposure to low levels of ionizing radiation comes from the national research council committee on the biological effects of ionizing radiation report (BEIR VII) of the national academy of sciences (BEIR VII, 2006).

3.3Review of the Epidemiological Studies of Human Population including atomic bomb survivors, patient exposed to radiation form diagnostic and therapeutic medical studies, as well as studies form occupational exposures and form exposure due to releases of radioactive material into the environment

3.4 Review of Cumulative Exposure oif Dose In Multiples of Dose From A Simple Chest X-Ray And Corroding Cancer Risk

The evidence considered by BEIR VII comprise epidemiological studies of human populations, including atomic bomb survivor, patients exposed to radiation form diagnostic and therapeutic medical studies, as well as studies from occupational exposure and from exposure due to releases of radioactive materials into the environment (Royal, 2008).

Direct epidemiological evidence (A-bomb survivors and other groups) demonstrated that there is a linear relationship between risk of cancer and between about 50mSv and 2.5Sv,

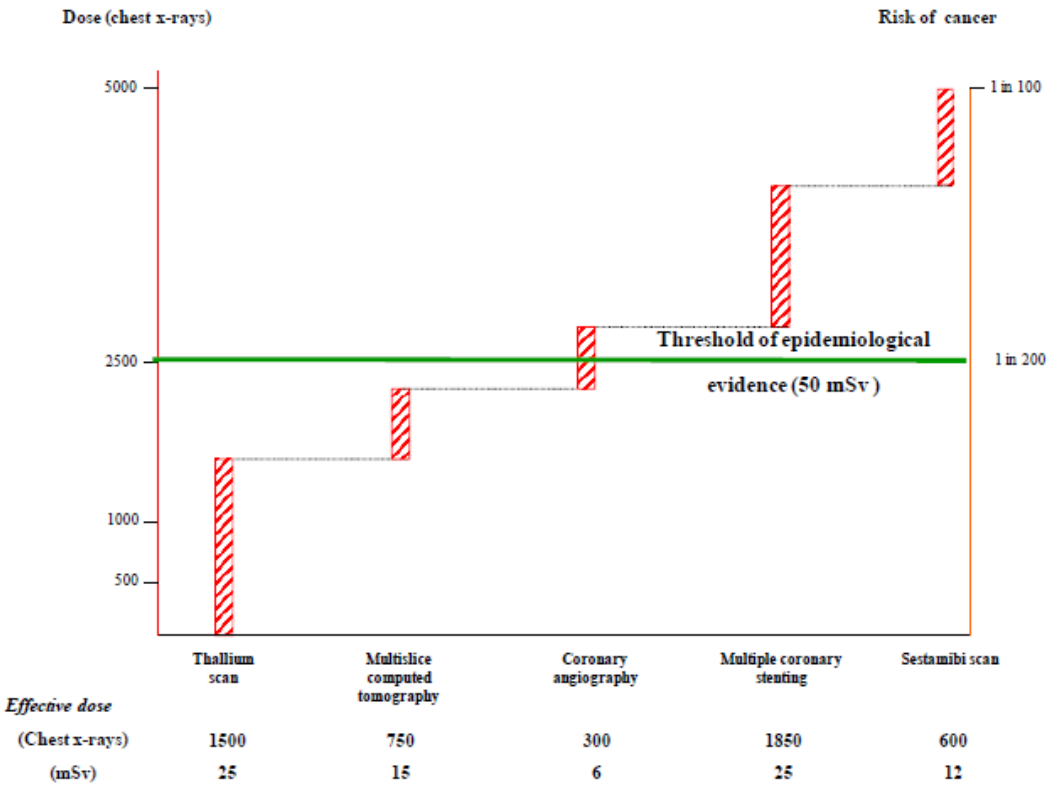
but the risk of cancer associated with lower dose remains uncertain, because the natural incidence of cancer in any population is high.

BEIR VII still reconfirmed that the LNT is the best model to estimate radiation risks, continuing to support the well established radiological concept that no radiation dose no matter how small can be considered completely safe.

BEIR VII indicated that a single adult population effective's dose of 10mSv result in a 1 in 1,000 life time risk of developing radiation induced solid cancer or Leukemia (BEIR VII, 2006). However approximately 42 people out of 100 are expected to develop cancer for other reasons (BEIR VII, 2006).

It is worth noting that many cardiac ionizing procedures have effective dose estimates in the range of 10 to 25mSv Bedetti *et al., (2008*) thus, it is not be uncommon for a patient to exceed the dose of 50mSv, even in a single hospital admission for a single problem, most commonly a suspicion of coronary artery disease.

Figure 3.1 graphical representation the cumulative exposure of dose in multiples of dose form a simple chest x-ray (y axis, left) and corresponding cancer risk (y axis, right cancer risk and radiation dose (in multiples of dose form a simple chest x-ray) for a typical cardiological patients undergoing to give radiological examinations.



Figures 3.1 Graphical representation the cumulative exposure of dose in multiples of dose form a simple chest x-ray (BEIR VII, 2006).

For instance, a 500 years man who undergoes one thallium scan stress test, one 64 slice computed tomography coronary angiography, one coronary angiography, and one coronary intervention would received an effective radiation dose of about 71mSV and thus would have an additional subsequent lifetime risk for developing cancer of about 1 in 150 patients.

Furthermore, it is very important to underline those children and young adults are especially vulnerable since they have more rapidly dividing cells and a greater life expectancy (BEIR VII, 2006). For example, the overall risk of developing cancer (incidence and mortality) from the same dose of radiation for a 1 year's old infant is 10-15 times greater than a 50 years old adult and female infants. Figures 3.2 show the estimated risk of cancer mortality as a function of age at exposure for both males and females.

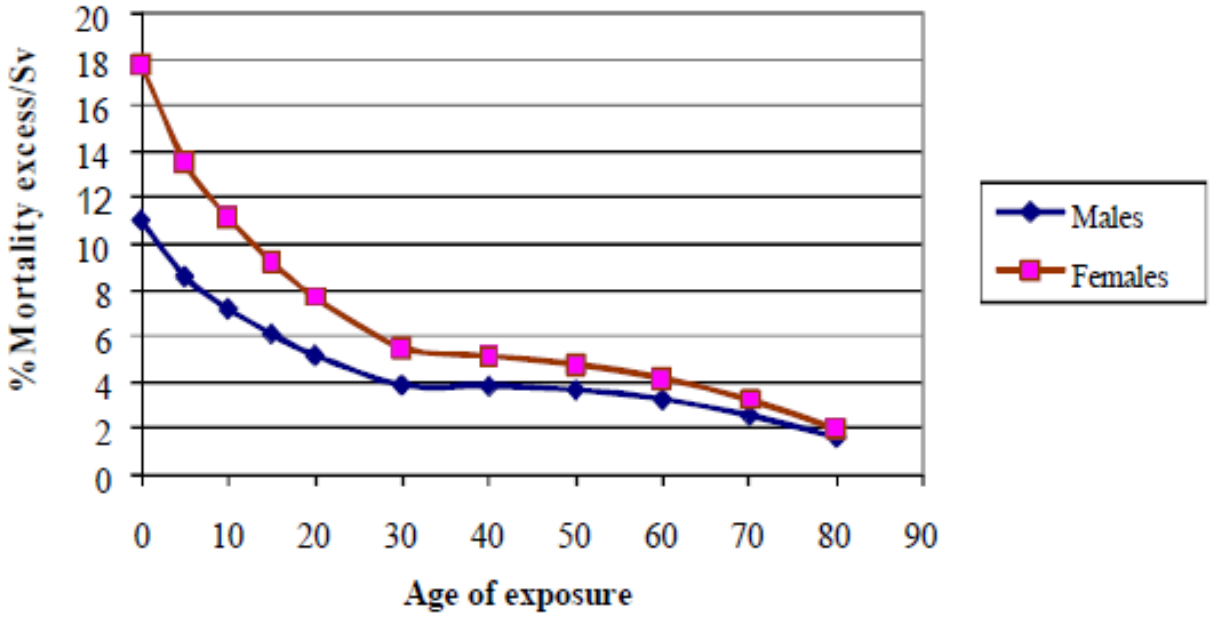


Figure 3.2 radiations induce risk of cancer on age and gender by using the BEIR VII Estimates (BEIR VII, 2006).

Therefore, alternative diagnostic modalities that do not involve the use of ionizing radiation should be considered in the evaluation of young individuals in order to minimize cancer risk Brenner *et al., (*2007).

CHAPTER FOUR

RESULTS AND ANALYSIS

4.1 RESULTS

Exposure carcinogenesis and heritable effects are the main risk with ionizing radiation. Other non-cancer adverse effects especially atherosclerotic cardiovascular and cerebrovascular risk can occur following high dose radiation therapy.

4.1.2 RADIATION RISK AT REGULAR INTERVAL PROGRESS WORLDWIDE IN ORDER TO REACH A BALANCED VIEW OF THE RISK INVOLVED.

The current consensus of regulatory bodies is that for radiation protection purposes the most appropriate risk model at low doses is the so-called linear no-threshold (LNT) model, without threshold safe dose.

4.1.3 THE EPIDEMIOLOGICAL STUDIES OF HUMAN POPULATION

The epidemiological studies of human populations, including atomic bomb survivor, patients exposed to radiation from diagnostic and therapeutic medical studies, as well as studies from occupational exposure and from exposure due to releases of radioactive materials into the environment.

4.1.4 CUMULATIVE EXPOSURE OF DOSE

cumulative exposure of dose in multiples of dose from a simple chest x-ray and corroding cancer risk.

4.5 ANALYSIS

Direct epidemiological evidence (A-bomb survivors and other groups) demonstrated that there is a linear relationship between risk of cancer and between about 50mSv and 2.5Sv, but the risk of cancer associated with lower dose remains uncertain, because the natural incidence of cancer in any population is high. BEIR VII still reconfirmed that the LNT is the best model to estimate radiation risks, continuing to support the well established radiological concept that no radiation dose no matter how small can be considered completely safe. BEIR VII indicate that a single adult population effective dose of 10mSv result in a 1 in 1,000 life time risk of developing radiation induce solid cancer or leukemia. However approximately 42 people out of 100 are expected to develop cancer for other reasons. It is worth noting that many cardiac ionizing procedures have effective dose estimates in the range of 10 to 25mSv thus, it is not be uncommon for a patient hospital admission for a single problem, most commonly a suspicion of coronary artery disease.

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATION

5.1 SUMMARY

The increasing exposure to medical radiation in western countries is a hot issue that the medical community needs to appreciate because it may likely result in the incidence of imaging related cancer in the future. Medical use of radiation is the largest man-made source of radiation exposure to the general population. According to the recent report on medical radiation received from clinical imaging has increased by 700% between 1980 and 2006.Many cardiac diagnostic or therapeutic testing, such as cardiac catheterization, CT and nuclear medicine scans accounting for >50% of imaging examinations, involve considerable exposure to ionizing radiation. A contemporary cardiac patient is exposed to a significant cumulative effective dose (a median cumulative effective dose of 60mSv per head) from multiple tests, often repeated needlessly.

The radiation is a process in which energetic particles or energetic waves travel through a vacuum, or through matter containing media that are not required for the propagation. Everyone is exposed to radiation on daily basis primarily from naturally occurring cosmic rays, radioactivity in the soil and radioactive element incorporated in the body, man-made sources of radiation such as x-ray or fallouts from historical nuclear weapon testing also contribute, but to a less extent about 80% of background radiation originated from naturally occurring sources with the remaining 20% resulting from man-made source. Radiation refers to the propagation of waves and particles through space and includes both electromagnetic radiations, atomic and sub-atomic, particle radiation;

electromagnetic radiation has a broad continuous spectrum of energy that includes visible light, radio waves etc. All electromagnetic radiation travel at the speed of light, particles radiation includes alpha particles, beta particles, neutrons, protons and heavy ions. The speed and energy of particles radiation depend on the sources of the radiation and any other subsequent interaction of the particles with other matter.

Radiation is classified into two, ionizing and non-ionizing radiation, according to whether it ionizes or does not ionize ordinary chemical matter. The radiation one typically encounters is one of four types: alpha radiation, beta radiation, gamma radiation and x-radiation. Neutron radiation is also encountered in nuclear power plant and high altitude flight and emitted from some industrial radioactive source. The biological effects of ionizing radiation are divided into two categories: deterministic and stochastic effects. Deterministic effects such as erythema or cataract have a threshold dose below which the biological response is not observed some cardiological interventional procedures with long screening times and multiple imaging acquisition (e.g percutaneous coronary intervention, radiofrequency ablation, etc) may gives rise to deterministic effects in both staff and patients. A stochastic effect is probabilistic event and there is no known threshold dose. The likelihood of inducing the effect but not the severity, increases in relation to dose and may differ among individuals. In fact, the effect, of low dose of radiation less than 50mSv do not cause on immediate problem to any body organ, but spread out over long periods of time after exposure. Damage to DNA which carries the genetic information in chromosomes in the cell nucleus, is considered to be the main initiating event by which radiation damage to cells result in development of cancer and hereditary discreas in the future children of exposed patients. Genetic effects are the

result of mutation produced in the reproductive cells of an exposed individual that are passed on to their offspring. These effects may show up as birth defects or other conditions in the future children of the exposed individual and succeeding generation.

X-ray imaging creates pictures of the side of your body. The images show the parts of your body in different shades of black and white. This because different tissues absorb different amounts of radiation. CT scans, also known as computed tomography scan, makes use of computed-processed combinations of many measurements, taken from different angles to produces cross sectional images (virtual “slices”) of specific areas of a scanned object without cutting. Fluoroscopy is an imaging modality that uses x-ray to allow real-time visualization of body structures. Magnetic resonance imaging (MRI) uses a large magnetic and radio waves to look at organs and structures inside your body. Health care professionals use MRI scans to diagnose a variety of conditions, from turn ligaments to tumors. MRIs are very useful for examining the brain and spinal cord. Nuclear medicine is a branch of medical imaging that uses small amounts of radioactive materials to diagnose and determine the severity of or treat a variety of diseases, including many types of cancer, heart disease, gastrointestinal, endocrine neurological disorders and other abnormalities within the body. Because nuclear medicine procedures are able to pinpoint molecular activity within the body, they offer the potential to identify disease in its earliest stages as well as a patient’s immediate response to therapeutic interventions. This project is aimed on reviewing the risk and effects of cardiac ionizing radiation, the clinical risk of medical ionizing radiation exposure, the risk at regular interval progress worldwide in order to reach a balanced view of the risk involved, the epidemiological studies of human populations, including atomic bomb survivors, patient

exposed to radiation from diagnostic and therapeutic medical studies as well as studies from occupational exposures and from exposure due to releases of radioactive material into the environment, cumulative exposure of dose in multiples of dose from a simple chest x-ray and corroding cancer risk. Exposure carcinogenesis, teratogensis and heritable effects are the main health risk with ionizing radiation. Other non-cancer adverse effects especially atherosclerotic cardiovascular and cerebrovascular risk can occur following high dose radiation therapy. Direct epidemiological evidence demonstrated that there is a linear relationship between risk of cancer and between about 50mSv and 2.5Sv, but the risk of cancer associated with lower dose remains uncertain, because the natural incidence of cancer in any populations is high.

5.2 Conclusion

Biomarker in the assessment of radiation exposure support BEIR VII estimates. The incorporation of molecular and cellular biomarkers (molecular epidemiology) into epidemiological studies has grown exponentially during recent years in order to better examine relationships between environmental hazards and human health effects.

The use of biomarkers is expected to identify important mechanistic insight into the pathogenesis of disease processes and reduce the time gap exposure and recognition of disease relevant effects.

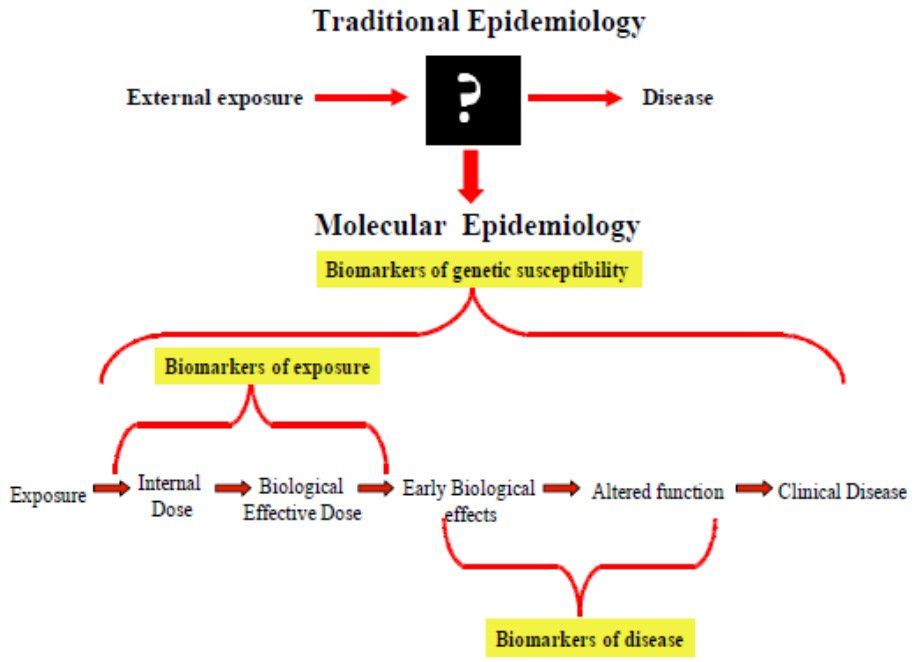


Figure 5.1 Biomarkers

Figure 5.1 biomarker are the key elements of molecular epidemiology and may open the "black box" form exposure to disease. One of the goals of molecular epidemiology studies is to use biomarkers in order to develop new and more effective strategies to reduce risk, such as exposure monitoring, health surveillance and individual risk characterization (Vineis *et al.,* 2007).

Different biomarkers reflecting exposure to and early effects of carcinogens, as well as individual genetic susceptibility to them, have become available and are being applied in population based (molecular epidemiology).

Biomarkers of early effect with relevance to the carcinogenic process include the evaluation of chromosomal DNA damage in peripheral blood lymphocytes in the form of chromosome aberrations and micronuclei (Andreassi, 2004). During recent years, indeed, large studies have provided consistent evidence that high levels of chromosomal DNA damage in peripheral blood lymphocytes are early predictors of cancer risk (Hagmar *et al.,* 1998).

The use of chromosomal biomarkers may assist in the difficult task of assessing the risk of radiation induced oncogenic effects. As such, they can complement classic epidemiological studies that use disease endpoints and require millions of people followed up for several decades.

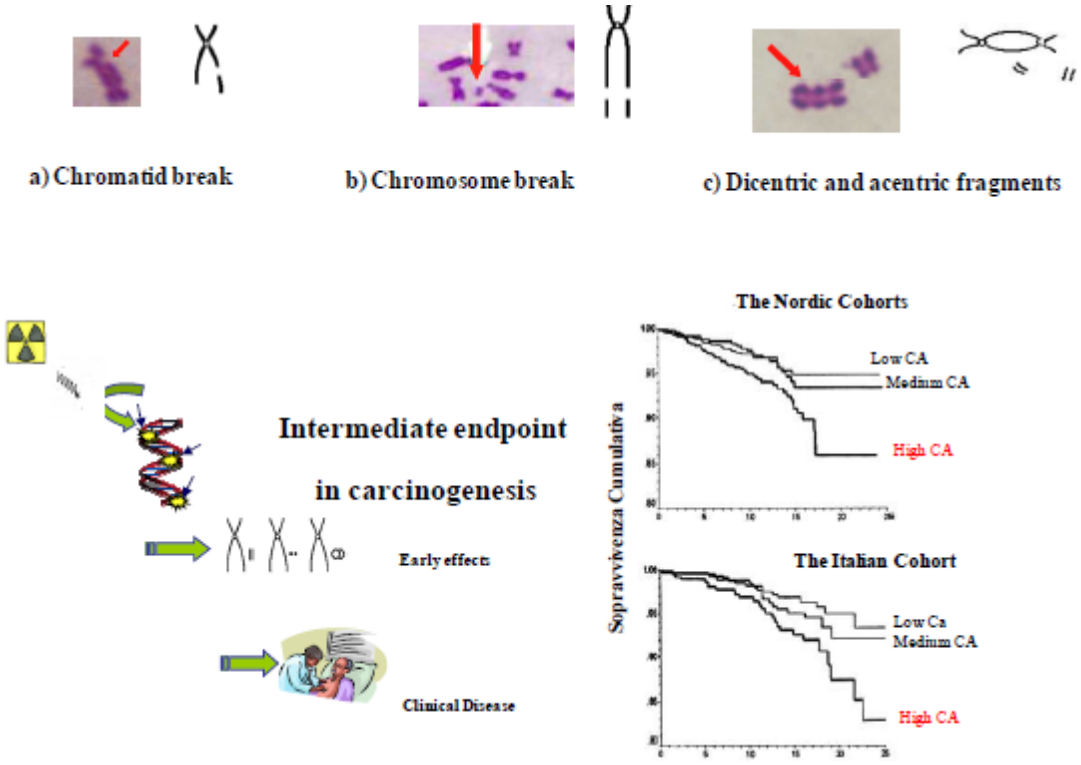


Figure 5.2 chromosomal aberrations in peripheral blood lymphocytes: biomarkers of early effect and cancer risk assessment (Hagmar *et al.*, 1998).

Indeed, it was recently used chromosomal biomarkers as intermediate endpoint in carcinogenesis in order to assess the potential risk due to cardiac catheter based fluoroscopic procedures, magically in the line of research needs as outlined by BEIR VII report on 2006 and by the white paper of the American college of radiology on effects of medical radiation released on 2007. The results corroborated the current radioprotection assumption that even modest radiation load can damage the DNA of the cell.

Invasive cardiovascular procedures can damage the DNA of the cell to be detectable acutely and in the long term as increased chromosomal DNA damage in circulating lymphocytes that represent on intermediate endpoint of cancer (Andreassi *et al.*, 2007).

Importantly, we observed that the lifetime exposure of a young adolescent with congenital heart disease in the range of 20mSv is associated with a dramatically 200% increased frequency of chromosomal DNA damage when compared to age-and sex-matched control subjects (Andreassi *et al.*, 2006).

Furthermore, we also showed that contemporary interventional cardiologists have an increased rate of chromosomal somatic DNA damage, reflected in higher frequency of micronuclei versus clinical cardiologists (Andreassi *et al.*, 2007).

Actually, interventional cardiologists have a per-capita per year exposure two to three times higher than that of radiologists (Vano *et al.*, 2006).

Cumulative doses after 30 years of working life can be as high as 100 to 250mSv, corresponding to a whole body dose equivalent to 5,000 to 12, 500 chest x-rays. This exposure gives an estimated life time attributable risk of cancer incidence in the range of 1 cancer in 100-1 in 200 exposed subject (Venneri *et al.*, 2009).

However, the amount of the damage varies and is only weakly related to the duration of professional exposure, suspecting that an individual predisposition may play an important role in the cellular response to radiation exposure.

Indeed, it is believed that genetic factors may play a crucial role in cellular responses to radiation and those common single nucleotide polymorphisms (SNPs) in DNA repair genes can lead to heritable predisposition to cancer. Accordingly, considerable effort is being expended in the search for SNPs involved in the different DNA repair pathways, including base excision repair (BER) pathway and double strand break repair process (DSB), which might act as cancer susceptibility genes (Au *et al.*, 2006).

Interestingly, we recently found harbouring two or more risk alleles of DNA repair genes, contribute to chromosomal DNA damage levels in interventional cardiologists suggesting that the risk estimates at the population level can be highly inaccurate at the individual level (Andreassi *et al.,* 2009).

A significant association between breast cancer risk and genetic polymorphisms has been also reported among women exposed to low levels of ionizing radiation form medical procedures (Milikan *et al.,* 2005).

Subgroups of women, who are carriers of mutation in DNA repair genes including BRCA-1 and BRCA-2, showed a significantly increased breast risk associated with exposure to diagnostic x-rays, especially to the chest (Andrieu *et al.,* 2006).

5.3 Recommendation

Therefore, the application of biomarkers in molecular epidemiological researches constitutes a promising new strategy for enhancing exposure assessment as well as for a better understanding of the mechanism of action and dose response relationship for ionizing radiation and human cancer.

In general, there is a need to continue epidemiological as well as to integrate these investigations with laboratory studies in order to provide new insight in low radiation risk, particularly encountered in modern medicine.

Future molecular epidemiologic studies incorporating genetic polymorphisms and biomarkers of early effects provide the rationale for identifying at risk susceptible or resistant subpopulation in order to develop better radiation protection programmes.

Medical imaging is the largest controlled source of radiation exposure to pupation, and its most important determinate is the ordering healthcare provider.

Therefore Physician education should emphasize that cardiac imaging studies that expose patients to ionizing radiation should be ordered only after though full consideration of the potential benefit to the patient and in keeping with established appropriateness criteria considerations should include options for answering the clinical question at hand by means that do not use ionizing radiation of choosing the type of study that exposes the patent to lowest amount of radiation.

- The risks of mission important diagnose imparted by no performing appropriate diagnostic imaging studies because of radiation dose concerns should be considered.

- Healthcare provider should diligently review patent records including those from other medical institutions, to ensure that imaging studies that use ionizing radiation are not repeated needless.
- Healthcare provider should discuss the risks and benefits of planned imaging procedures with patents when even practical and appropriate.

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