Biological Effects and Medical Applications of Radiation

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Abstract

With the development of radio-therapeutic oncology, computer technology and medical imaging technology, radiation therapy has made great progress[24]. Radiation's benefits were initially realised in the use of X-rays for medical diagnosis, and then later with the discovery of radiation and radioactivity. The desire to take advantage of the medical benefits led to a reasonable assessment of the hazards and resulting consequences. Only the most evident effects of large doses of radiation, such as radiation burns, were noticed in those early days, and protection efforts were concentrated on preventing them, mostly for practitioners rather than patients[8]. In this term paper we will be discussing about the various sources of radiation, medical applications of radiation and how the damage produced by ionizing radiation in biological molecules affects the body cells.

1 Introduction

Modern techniques in nuclear medicine have proven to be powerful tools for diagnosis and treatment of an increasing number of diseases[20]. However, they all add to the patient's radiation exposure. As a result, constant attention should be paid to reducing the radiation dose involved. The risks associated with a specific nuclear procedure should be known in order to weigh its advantage against its disadvantages[4]. These risks depend on the dose and dose and dose-effect relationship. The discipline involved in dose calculation is called dosimetry. The combination of the results of dosimetry and dose-effect relation allows the estimation of the risk associated with a certain nuclear procedure[23].

People would appreciate that radiation has quiet and useful applications in our daily lives once they understand it. New difficulties in terms of worldwide levels of radiation exposure continue to emerge, new biological information on the impacts of radiation exposure is becoming available[25].

2 Sources of Radiation

As a part of living on earth, people are exposed to radiation from various sources every day. Radiation is the energy that travels through space, in the form of particles or electromagnetic waves such as radio, microwaves, infrared, visible light, ultraviolet, alpha particles, X-rays and Gamma-rays etc[25]. According to [19] these sources of ionizing radiation could be from natural background radiation such as radon and thoron, cosmic and terrestrial radiation, or man-made radiation such as those from xray or nuclear medicine (NM) procedures.

2.1 Natural Radiation

The assessment of the natural radiation doses from natural sources in human is of particular importance natural radiation is the largest contributor to the collective dose of world population[7]. The natural radiation sources are classified into:

- External Irradiation
- Internal Irradiation

2.1.1 External Irradiation

1. **Cosmic Radiation:**

   This is simply the radiation from the sun and stars. Flying based at high altitudes much frequently and for long duration will attract extra cosmic radiation exposure[11].

2. **Terrestrial Radiation:**

   This is the radiation due to the presence of radioactive materials such as uranium, thorium, and radium that exist naturally in soil, water and rocks. Essentially air contains radon, which is responsible for the dose from natural background sources, and all organic matter (plant and animal) also contains radioactive carbon and potassium[14]. However, the dose from these sources varies in different parts of the world, but locations with higher soil concentrations of uranium and thorium generally have higher doses. Therefore, the background radiation levels vary in certain areas due to geological differences and sometimes the exposure can be more than 200 times higher than the global average[22].

2.1.2 Internal Irradiation

From birth to death, this sort of radiation is caused by the internal composition of human bodies, which includes radioactive potassium-40 and carbon-14[9].

1. **Artificial (Man-made) Radiation:**

   The following are examples of man-made radiation:

   - Medical techniques such as diagnostic x-rays, nuclear medicine, and radiation therapy expose people to radiation. Consumer products, such as building materials, combustible fuels (gas and coal), television, and cell phones, are also included in this category.
   - Radiation from nuclear sites, which account for less than 0.01 percent of the average annual dose, as well as exposure from radioactive materials shipment and residual fallout from nuclear weapons testing and accidents like Chernobyl.

3 Dosimetry

The science of "dosimetry" is the measurement, calculation, or combination of measurement and calculation used to calculate radiation exposure. Radiation dosage is also known as "absorbed dose," which is defined as the quantity of radiation energy deposited in tissue divided by the tissue's mass. The most important physical component that impacts the response of tumours and the rest of the body to radiation is the absorbed dosage[13]. When a subject is exposed to radiation, dosimetry provides a method of calculating parameter for risk estimation. Thereby two different situations have to be distinguished: irradiation from an external source and irradiation from activity present inside the body. These two situations require a different approach.

External Source

The following aspects are involved in these calculations:

1. the strength or activity of the radioactive source;
2. the exposure of the subject to such radiation;
3. the dose absorbed by the different tissues;
4. the biological effectiveness of the type of radiation;
5. the weighting of the seperate organs

These items will all be discussed subsequently in this section. Since the introduction of the Systeme internationale (SI) as the basis for quantification of scientific measurements, the units for most radiation quantities have been changed[12]. The relation between those SI units and their corresponding conventional is indicated in Table 1

Measurement	Description	SI unit	Conventional unit	Relationship
Radioactivity	Nuclear transformation (disintegrations per second)	Becquerel (Bq)	Curie (Ci)	1 Bq = 2.7x10^{-11} Ci, 1 Ci = 3.7x10^{10} Bq
Exposure	Charge produced in air by γ - or X-rays	Coulombs per kilogram of air (C.Kg^{-1})	Roentgen (R)	1 C.Kg^{-1} = 3876 R, 1 R = 2.58x10^{-4} C.Kg^{-1}
Exposure rate	Observed dose rate in air from a sealed source at a distance of 1m from source	C.$Kg^{-1}.s^{-1}$	R.s^{-1}	1 C.$Kg^{-1}.s^{-1}$ = 3876 R.s^{-1}, 1 R.s^{-1} = 2.58x10^{-4} C.$Kg^{-1}.s^{-1}$
Absorbed dose	Amount of energy imparted to matter	Gray (Gy)	Rad	1Gy=100 Rad, 1 Rad=0.01Gy
Dose equivalent	Absorbed dose multiplied by modifying factors	Sievert (Sv)	Rem	1 Sv=100 Rem, 1 Rem=0.01 Sv

Table 1: Comparison of common radiation terms in System Internationale (SI) and conventional units

- Activity: The measure of the activity of a radioactive source is the number of disintegration per second. For many years this activity was expressed in Curie (Ci), defined as activity of one gram of radium. Since the introduction of the SI-units, the unit for radioactivity is Becquerel (Bq). It is defined as one integration per second.
- Exposure: The exposure of a subject to radiation depends on the intensity of radiation where that subject is. It is related to the source strength, the distance between the source and the subject, the type and energy of radiation and absorbing properties of the material between the source and subject. The unit for exposure is Roentgen (R) or Coulombs per kilogram of air (C.kg-1).
- Absorbed Dose: The absorbed dose (D) is represented by the amount of energy imparted to matter. It is proportional to the exposure and is dependent on the type of matter and the properties of radiation. The SI-units of absorbed dose is the Gray (Gy) corresponding to J.kg-1. The absorbed dose is usually calculated seperately for various organs.
- Dose Equivalent: The effect of radiation is not only determined by the absorbed dose but also by the biological effectiveness of the radiation, given as the quality-factor Q. When this has been taken into account, the dose equivalent is obtained. The SI-unit of dose equivalent is Sievert (Sv). The biological effect of a given dose equivalent is independent of the type of the radiation.

Internal Source
Irradiation from activity inside the body will always be in-homogeneous[21]. The dose equivalent, therefore, should be calculated separately for each organ. It depends on

1. the number of disintegration inside this specific organ
2. the effective dose equivalent per disintegration

1. the number of disintegrations: The resorption, the distribution and the effective half-time (T1/2eff) of a radionuclide (radiopharmaceutical) within a specific organ, determine the number of disintegrations inside this organ. The resorption

of radionuclide depends on its chemical form and the way the radionuclide is administered. This administration may be performed, for example orally and intravenously. The distribution is determined by the chemical properties of the unbound radionuclide. Unbound 59Fe, for example, will be incorporated in precursor cells within the bone marrow, whereas 123I will be accumulated within the thyroid gland. The radionuclide may also be bound to specific cells or other organical structures. When 111In is labeled to platelets, the majority of administered 111In will be sequestered within the spleen and the liver, whereas leucocytes labeled with 111In will be localized at the site(s) of infection(s) or abscess(s). The T1/2eff is the resultant of the nuclear half-life and the biological half-life of radionuclide within this organ. The nuclear half-life is fixed but the biological half-life is determined by the rate of clearance of the radionuclide by the organ involved. This will be influenced by the rate of metabolism of the body in general and by possible diseases of a specific organ[1].

2. the effective dose equivalents per disintegration: The effective dose equivalent per disintegration depends on the amount of energy imparted to a certain organ and the biological effectiveness of the radiation. The former is particularly determined by the size of the organ. The biological effectiveness is given by the quality factor, Q, as explained above. The use of an alpha-emitter, for example, leads to a high effective dose equivalent per disintegration. Subsequently, the total EDE can be estimated from the dose equivalent for each seperate organ on the analogy of the calculations for inhomogeneous external irradiation. In general, a low T1/2eff and low energy per disintegrations will result in the smallest radiotoxicity[16].

3.1 Why it is important?

Absorbed dose determines the extent to which tumors and normal tissues are affected by radiation. The higher the absorbed dose to tumors, the more cells will be killed by radiation and the greater the likelihood of a cure. However, the higher the absorbed dose to normal tissues, the more likely and severe may be the undesirable toxic side-effects of the radiation. An important advantage of radiopharmaceutical therapy is its ability to irradiate and effectively treat tumors throughout the body; at the same time, some irradiation of normal organs is unavoidable. Therefore, the role of radiation dosimetry in targeted radionuclide therapy is to determine specifically, for each patient, the administered amount of the radiopharmaceutical that will most effectively treat the patient's disease while avoiding absorbed doses that damage normal tissues. Individualized radiation dosimetry is critical for planning the most effective and safest targeted radionuclide therapy for each patient[3].

3.2 Radiotoxicity

Depending on the T1/2eff of a radionuclide and the type of emitted radiation the EDE or different radionuclides per Bq administered extends over an interval of five orders of magnitude, from 0.00015 to 20 mSv.MBq-1. This resulted in the subdivision of radionuclides into four categories. The radionuclides most frequently administered are 51Cr, 55Fe, 57Co,58Co, 59Fe,67Ga, 99mTc, 111In, 123I. 125I, 131I, 133Xe, 201Tl. In Table they are classified in the categories mentioned (No radionuclides are generally applied from category 1). The maximum dose allowed for the radionuclides from different categories is also given[23].

Group	Example allowed (Bq)	Maximum Activity
2	114mIn,125I,131I	5.10^{-4}
3	55Fe,57Co,58Co,59Fe,67Ga,111In,123I	5.10^{-5}
4	51Cr,99mTc,133Xe,201Tl	5.10^{-6}

Table 2: Several radionuclides classified by their radioactivity

3.3 Biological Effects and Dose-Effect Relation

In 1901, Becuerel discovered that radiation could cause a red and blistered skin. Since then, many somatic effects have been associated with the exposure to radioactivity. The main examples of such potential harms are leukemia, solid tumours and mental retardation. Besides somatic radiation effects there are hereditary effects. It is assumed that all biological effects have a different dose-effect relation. Irradiation by atomic weapons, industrial pollution and medical procedures from the main sources from which the information about dose-effect relations has been obtained[17]. With calamities, the exposure to radioactivity generally leads to a high absorbed dose. The biological effects that occur provide information about the dose-effect relation at high dose. This may not just be extrapolated to low dose effects. Studies performed among people who received a low dose, for example those living in areas with increased natural radiation levels, have never demonstrated measurable biological effects, partly because of the high natural incidence of most radiation-associated diseases.

4 Biological Effects

The somatic effects that have been ascribed to radioactivity are various types of cancers such as leukemia, lymphomas, solid tumours like breast cancer and colon cancer, mental retardation, growth retardation, impaired fertility, skin cancer, bone marrow depression, functional impairment of the central nervous system and cataract. Radiation may also cause chromosome aberrations which will be ex pressed in the descendants of the exposed subjects; they are described as the hereditary effects.

Fatal cancers must be differentiated from non-fatal cancers with regard to the effects of radiation. The risk factors for all cancers are of course higher then those for fatal cancers. The mortality rate is about 5-10% for thyroid cancer, 40-50% for breast cancer and 90-100% for lung cancer. The incidence of all cancers after exposure of the general population comes to about three times the incidence of fatal cancers.

In 1977, the effects of radiation were divided into stochastic (random) effects and non-stochastic (non-random) effects[2]. It can be broken into two groups according to how the responses (symptoms or effects) relate to dose (or amount of radiation received). Stochastic effects are defined as having no threshold in dose and no change in severity with dose. Only the incidence is a function of dose. Non-stochastic effects do have a threshold and change in severity with dose. The certainty that radiation effects can be rigidly categorized into one or other group is falling into disfavour. Whereas the cancers and the hereditary effects are both still regarded as being stochastic, the non-stochastic effects have been subdivided into three classes. The relevance of this modification is the former opinion that non-stochastic effects could be completely prevented because of their threshold. It now appears, however, that no threshold may exist for several non-stochastic effect such as the reduction of intelligence quotient (IQ) from fetal irradiation. All possible examples of stochastic and non-stochastic effects are summarized in Table 3. The question mark after each example emphasizes the uncertainty of well it conforms to the rigid definition of its classification. The first category consists of exposure to low doses of radiation over an extended period of time producing chronic or long term effects (Stochastic) while the second category represents exposure to high doses of radiation over short periods of time producing acute or short term effects (Deterministic). The high doses tend to kill cells, while low doses tend to damage or change them. High doses can kill so many cells that will lead to damage of tissues and organs. This may result to a rapid whole body response often called the Acute Radiation Syndrome (ARS)[25]. The effect of radiation is dependent on many factors including:

- The type of radiation (alpha, beta or gamma)
- The amount received
- The rate at which it is received
- Which part of the body is exposed
- Whether the exposure is chronic (regular, low doses) or acute (short time, high dose)
- The age of the irradiated person.

4.1 High dose sources

Several tragic calamities have provided important information and new insights into this subject. The studies of 90,000 survivors of the Hiroshima and Nagasaki atomic bombs in particular have been very influential. In Hiroshima the effects of the 235Uranium bomb were mainly due to neutrons, whereas in Nagasaki the effects from the 239Plutonium bomb were mainly due

to γ -rays[15]. A tentative dosimetry as developed in 1965, known as T65D, has been used for risk estimation since then. A reassessment of the data, including a longer follow-up, has resulted in a revised dosimetry: DS 86. Similarly, the accident at the Chernobyl nuclear reactor in 1986 is expected to provide scientists with many data and consequently, as a side-effect, an undesired but valuable opportunity to study the health effects of radiation.

Dose-effect relation	Threshold	Severity of effect varies with dose	Possible examples
Stochastic	No	No	Cancers? Mutations?
Non-stochastic Class 1	Yes	Yes	Cataracts? Impaired fertility? Anemia?
Non-stochastic Class 2	No	Yes	IQ-reduction? Growth retardation? Lethal mutations?
Non-stochastic Class 3	Yes	No	Skin cancer?

Table 3: Possible examples of stochastic and non-stochastic effects

4.2 High dose low dose

Information is only available about the dose-effect relation at high dose. On the other hand, it is obvious that the absence of radiation will cause no radiation related biological effect. The vital question is how to interpolate between these data. The ICRP uses a linear model, assuming a linear dose response with no threshold, because it is the most cautious, in preference to linear quadratic or quadratic relations. The Society of Nuclear Medicine (SNM) and the American College of Nuclear Physicians (ACNP) question the validity of the ICRP guidelines. In their opinion the ICRP erroneously makes the assumption that exposure to low dose rates and high dose rates are equally hazardous. A dose-rate effectiveness factor (DREF) of 3 has been adopted by the National Radiological Protection Board (NRPB) to reduce high dose risk estimates to those appropriate for low-dose conditions. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) concluded that the carcinogenic effects of low LET-radiation are generally smaller at low dose compared with those at high dose. The reduction factors will vary with dose and with organ system but will generally fall within the range of 2 to 10. All these extrapolations from. high-dose irradiation towards low-dose irradiation effects are still complicated and full of assumptions. But from an epidemiological point of view it is almost impossible to relate cancer incidences to radiation exposure at the very low dose level, due to the low values of risk coefficients and due to the high "natural" incidence of possible "radiation related" diseases.

It is even postulated that in the range of 0.1-5 mSv of low LET-radiation there might be an overall beneficial effect[10]. An improvement of cellular radical detoxifi cation was observed in mouse bone marrow cells. Another adaptive response pertaining to improved DNA repair, was reported for human lymphocytes. It is speculated that improved radical detoxification and improved DNA repair may reduce the probability of spontaneous carcinogenesis. These putative stimulatory effects have been given the name "radiation hormesis".

Despite its doubtless potential of harm at high doses, there is no proof that there is harm to man at low level exposure with individual cells experiencing a single elemental dose. Because irradiation induces both adaptive responses and detriments, one type of effect may not simply be added to another in assessing risk to tissue[23].

5 Medical Applications

Medical use of nuclear radiation is quite common in today's hospitals and clinics. One of the most important uses of nuclear radiation is the location and study of diseased tissue[18]. This application requires a special drug called a radio-pharmaceutical. A radio-pharmaceutical contains an unstable radioactive isotope. When the drug enters the body, it tends to concentrate in inflamed regions of the body. (Recall that the interaction of the drug with the body does not depend on whether a given nucleus is replaced by one of its isotopes, since this interaction is de-

termined by chemical interactions.) Radiation detectors used outside the body use nuclear radiation from the radioisotopes to locate the diseased tissue. Radio-pharmaceuticals are called radioactive tags because they allow doctors to track the movement of drugs in the body. Radioactive tags are for many purposes, including the identification of cancer cells in the bones, brain tumors, and Alzheimer's disease (Figure 1). Radioactive tags are also used to monitor the function of body organs, such as blood flow, heart muscle activity, and iodine uptake in the thyroid gland.

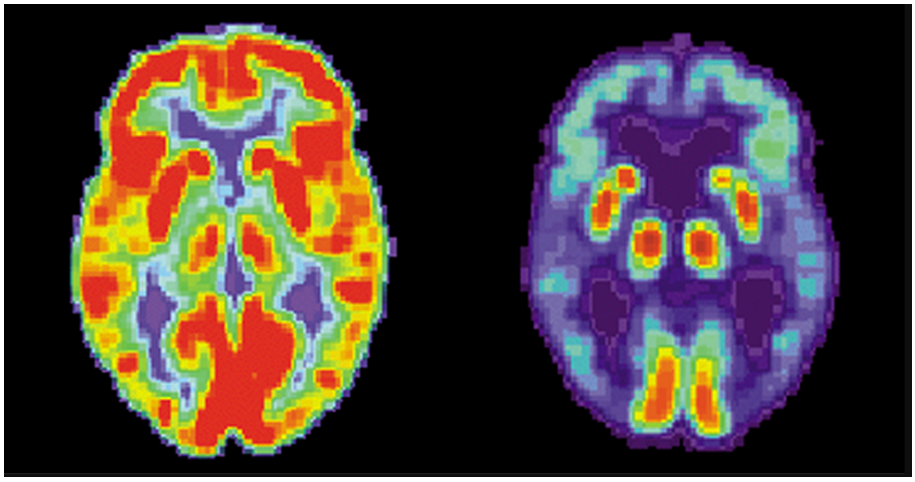

Figure 1: These brain images are produced using a radio-pharmaceutical. The colors indicate relative metabolic or biochemical activity (red indicates high activity and blue indicates low activity). The figure on the left shows the normal brain of an individual and the figure on the right shows the brain of someone diagnosed with Alzheimer's disease. The brain image of the normal brain indicates much greater metabolic activity (a larger fraction of red and orange areas). (credit: modification of works by National Institutes of Health)

Table 4 lists some medical diagnostic uses of radio-pharmaceuticals, including isotopes and typical activity (A) levels. One common diagnostic test uses iodine to image the thyroid, since iodine is concentrated in that organ. Another common nuclear diagnostic is the thallium scan for the cardiovascular system, which reveals blockages in the coronary arteries and examines heart activity. The salt TlCl can be used because it acts like NaCl and follows the blood. Note that Table 4 lists many diagnostic uses for 99mTc , where "m" stands for a metastable state of the technetium nucleus[5]. This isotope is used in many compounds to image the skeleton, heart, lungs, and kidneys. About 80 % of all radio-pharmaceuticals employ 99mTc because it produces a single, easily identified, 0.142-MeV ray and has a short 6.0-h half-life, which reduces radiation exposure.

Procedure	Isotope Activity (mCi), where 1mCi=3.7×107Bq	Procedure	Isotope Activity (mCi), where 1mCi=3.7×107Bq
Brain scan		Thyroid scan	
99mTc	7.5	131I	0.05
15O (PET)	50	123I	0.07
Lung scan		Liver scan	
133Xe	7.5	198Au (colloid)	0.1
99mTc	2	99mTc (colloid)	2
Cardiovascular blood pool		Bone scan	
131I	0.2	85Sr	0.1
99mTc	2	99mTc	10
Cardiovascular arterial flow		Kidney scan	
201Tl	3	197Hg	0.1
24Na	7.5	99mTc	1.5

Table 4: Diagnostic Uses of Radiopharmaceuticals

6 Conclusion

As explained in this review there are still many uncertainties and assumptions concerning the biological effects of radiation [6]. Nevertheless, several committees and organizations, in particular the ICRP, have offered a general guidance for calculating the EDE attributed to nuclear medicine procedures and for dose limits. On the other hand, the clinician should always judge the importance of the information to be obtained in a specific individual case. It is this responsibility that he or she should be aware of.

Moreover, the aim should always be to reduce the absorbed dose as much as possible. This can be achieved by the application of prolonged counting times only. The use of other detecting system may also result in decreased radiation doses. The well-type Ge semiconductor detector, for example, has proven to be applicable in semi-in vivo nuclear medicine procedures. The high sensitivity and the high energy resolution of this detector has led to a considerable reduction of the EDE in the semi-in vivo procedures involved. This reduction varied from 6 to more than 100 times. More study is necessary to create new possibilities for dose reduction, in particular in pure in vivo procedures[23].

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