MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Clinical Radiology & Imaging Journal
ISSN: 2640-2343

Radiation Protection Issues in Clinical Research Involving X-Ray Diagnostic Radiology Procedures

Fatukasi J[1]*, Olowookere C[2], Olatunji M[3] and Osho S[4]

[1]Associate Professor, Department of Radiology, University of Medical Sciences, Nigeria
[2]Associate Professor, Department of Physics University of Medical Sciences, Nigeria
[3]Lecturer, Department of Physics, University of Medical Sciences, Nigeria
[4]Senior Lecturer, Department of Radiology, University of Medical Sciences, Nigeria

Essay
Volume 7 Issue 1
Received Date: May 22, 2023
Published Date: June 26, 2023
DOI: 10.23880/crij-16000202

***Corresponding author:** Joseph Fatukasi, Associate Professor, Department of Radiology, University of Medical Sciences, Ondo State, Nigeria, Email: josephfatukasi@gmail.com

Abstract

Aim: To review radiation protection issues in clinical diagnostic studies that involves the use of x-rays.

The Issue: X-rays imparting low dose have some dominance in the use of ionising radiation (IR) in clinical radiological investigations. In good clinical diagnostic practice, with radiation effects anticipated to be wholly stochastic, it is simply not possible to be specific about risks to health other than to acknowledge an anticipated increase in probability with dose. Difficulties in making an assessment of risk can be further compounded given possible cumulative effects from previous exposures and from varying clinical state.

Scientific Considerations: Clinically focused research involving IR and subjects (reviewed by ethics committees and other parties) necessarily involves assessment of the study protocol. In addition to the embodiment of radiation protection principles, the protocol must conform to the general ethical principles of beneficence, prudence, justice and dignity, all of which are important. The protection aspects arising from the use of radiation needs to be assessed by radiation experts, the safety of study participants needing to be weighed against the necessity for the study. This information must be fully explained to the participant as part of the process of seeking consent. In obtaining consent, the participant information sheet must be of an appropriate quality of language and possible specific risks provided in a transparent manner.

Conclusion: In clinical studies that involve the use of IR, the study protocol must contain all relevant radiation protection measures. It is important that review of the protocol should involve IR experts.

Keywords: Ionising Radiation Effects; Biological Effects of Radiation; Research Ethics in Radiation Exposure; Radiation in Pregnancy; Radiation in Children; Radiation in the Immunocompromised

Abbreviations: IR: Ionising radiation; CT: Computed Tomography; PIS: Participant Information Sheet; ALARA: As Low As Reasonably Achievable; ERR: Excess Relative Risk.

Introduction

Ionising radiation (IR), invisible and odourless, can penetrate structures (human tissues included), interacting

to a greater or lesser extent with the media through which it travels, a matter defining the extent of absorption and predicating dose. From within the electromagnetic spectrum the x-and gamma-ray IR involves a broad energy range. The environment, inclusive of humans and all living things, is continuously exposed to ionizing radiation, natural alone in the absence of anthropomorphic sources. In the case of anthropomorphic sources, the source systems are often designed for specific purposes, for instance the x-ray facilities of diagnostic radiology. Clinical x-ray diagnostic procedures have been estimated to be responsible for over 90% of the total radiation exposure of the population [1].

Radiation exposures of < 100mGy (true for most diagnostic radiology procedures) are classified as being low. Conversely, exposures of >1Gy (often from radiotherapy) are classified as high. Both medical diagnostic and environmental exposures (including cosmic sources) lie within the realm of low radiation exposure [2,3].

Broadly, the risks of IR exposure result from the development of harmful reactions, including detrimental effects from stochastic events (chance phenomena), also from exposure values that are known to cause particular harm. The harmful reactions are dose dependent, being expected to occur in high exposure scenarios, including as damage to the skin, reticuloendothelial, gastrointestinal and neuro-vascular tissues, occurring within a few days to weeks post-exposure. The stochastic (random) effects are usually due to cellular molecular damage, potentially resulting in cancer and varieties of congenital and heritable anomalies manifesting after a lag period of 6-20 years following exposure. Low dose exposures rarely manifest in harmful reactions while the stochastic risks from an exposure may be compounded by the cumulative effect of previous exposures [1].

Manifestations arising out of the risk depend on the dose as well as the types of tissue. The risks of tissue adverse effects on health are greatest in tissues within which there are rapidly growing cells such as found in paediatric groups [4] as well as radiation sensitive organs such as the bulbs of the eye, thyroid and breast tissue, and gonads, all greatly vulnerable to ionising radiation damage [4]. Opinions on immunological effects of ionising radiation remain controversial, being either positive or negative [5-7].

In research, a study protocol must be prepared, including information on the radiation protection principles at play, with emphasis on the dose, rationale, methodology and appropriate participant information, all parts of the consent process [8].

This review will focus on biological effects of radiation, the focus being on clinical research using low dose x-ray diagnostic exposures, peculiarities of participant clinical states, ethical issues and the consent process, all of which need to be addressed. These are important ethical review components, invariably requiring the input of ionising radiation specialists.

General Biological Effects of Ionising Radiation

Following Rontgen's discovery of the X-ray in 1895, the adverse effects of these emanations were neither known nor thought of until clinical changes were observed, subsequently to be correctly attributed to the x-ray exposures. Clarence Dally, assistant to Thomas Edison, was recorded in 1896 to be using his wrist in an effort to perceive the heat generated by x-rays. Working with the rays led to erythema, hair loss and eventually to ulcerating wrist skin cancer; within eight years of working with x-rays he was dead. By 1911, over 90 cases had been documented. Moreover, radiologists from that time were noted to have a reduction in life expectancy and an increased incidence of leukaemia. Similar trends were noted in industries in were radioactive substances were being used [1]. From such experiences, it was later apparent that the changes were a result of the interactions of radiation with cells, rooted in their ability to ionise, creating chemical species (electrons, positive ions like H+ and free radicals), disrupting cellular water and cell chromosomes. Subsequent clinical features were noted to include focal inflammation and erythema changes, and eventually mitotic changes [9].

Large doses of radiation (>1Gy) will lead to cell interactions which may cause reduction in tissue cell division / multiplication. At reductions in the number of cells below a critical level, affected tissue/organ functions can be expected to be preserved. Above a critical cellular threshold, harmful changes lead to deterioration of organ/body function. These tissue effects, formerly known as deterministic, are now referred to as harmful tissue reactions, being likely to manifest at high radiation doses [1,9].

Following exposure to low doses of radiation, stochastic effects result. The effects may be abnormal multiplication of cells leading to cancer and/or modification of cell chromosomal DNA genetics, leading to lethal or inheritable congenital abnormalities [1,9].

Within the precautionary principle that assumes that any dose above background may cause harm, a radiation dose of 1mSv carries a relatively low cancer risk, at 1 in 10,000 [1]. Efforts to be more precise do not give consistent figures. In a 2001 study, British Radiologists were shown to be expressing lower cancer rates compared to estimates for those cases included within the Hiroshima and Nagasaki atomic bomb study [10]. In 2007, a large 15-country wide study [11] showed significant ($p < 0.002$) excess relative

risk (ERR) of 4.2 x 10-5 per mSv. The doses from Computed Tomography (CT) as used in diagnostic radiology are within the low dose (stochastic effect) range, a longitudinal study of the dose show a small but significant increased risk of malignancy, potentially also covering cumulative effects of previous exposures [12]. Despite these varying observations, the relatively low doses from CT examinations are seen to be associated with at least a small increase in cancer risk, albeit with stochastic effects in low-dose exposure remaining poorly understood [13,14].

Clinical Situations

The human body cells, tissues and organs have varying features and susceptibility to ionising effects of irradiation. Cells that are actively dividing and immature or poorly differentiated are more radiosensitive. These facts partly explain the increased ionising radiation risks (harmful reactions and/or stochastic effects) in clinical entities like pregnancy, embryo/foetus, paediatrics, gonads, haematopoeitic system, gastrointestinal mucosa, neuro vasculature, breasts and thyroid gland [9].

In general, most radio-diagnostic activities are in the low-dose exposure range meaning that tissue harmful reactions are not expected. However, in fluoroscopic procedures (diagnostic and/or interventional, as in angiography) radiation harmful reactions may manifest [15].

Radiation risks (lifetime radiation-induced cancer as well as heritable effects) decrease with age for both males and females [14,16]. In CT studies, women have been reported to have double the risk of radiation effects than men, believed to be associated with the radio-sensitivity of the female breast. Attempts to estimate the breast doses experimentally have resulted in widely varying results of 10-70 mGy. It is generally accepted that breast dose from CT is much greater than glandular tissue exposure in mammography. The risk is greatest for those who are in the less than 40 years of age group [12,17].

Young age may have a compounding effect in pregnancy, stochastic risk being greater in the young and for females [16]. While a pregnant mother may well be considered to benefit from a particular diagnostic radiology exposure, the foetus is known to carry risks such as congenital malformation, mental retardation, and radiation-induced cancer, the risk being up to three-times greater than for adults [18]. Compared to more mature individuals, post-exposure to radiation the cells of paediatric patients typically have greater opportunity to undergo cancerous transformation, since these cells are dividing more rapidly than in adults [4,14].

Immunological issues are equally important. Whether for low or high exposures, IR has a modifying and controlling influence on the cell contents, genes, cytokines, immunological cells, individual tissues and the organs [5-7]. Evidence from high exposure situations, such as in radiotherapy, cancer cells are known to elicit anti-tumour immune responses involving cell autonomous activities as well as intercellular communications. The late side effects from low radiation exposures have demonstrated radiation-induced cell-killing, bystander- (abscopal), inflammatory- and immunological effects. In a study reported by Nelson, et al. [5], exposure of rat ear cells to low doses of radiation caused a 30% and 10-15% reduction in adaptive immunity and blood cells respectively. With high radiation dose, the reductions were 70% and 65% respectively. Moreover, gene and cytokines expressions analysis of the radiated ear areas show increased chemo-attraction. These imply that immunological status decreases with increasing radiation dose and that lowered immunity situations may increase susceptibility to antigens following exposure to radiation [5]. Furthermore, these findings infer that ionising radiation immune modulation may result in positive or negative effects, depending on whether the patient has normal immune status or immunodeficiency (as for HIV or Covid 19 infected individuals) and if the IR enhances or depresses immunity.

Radiation Protection Aspects of Ethical Considerations

The Declaration of Helsinki, a World Medical Association document, contains the ethical principles of clinical research. Ethical assessment requires weighing risks against benefits. The researcher must also be aware of potential radiosensitivity of relevant tissue areas in the study [9,19].

Unlike pharmaceutical and related studies, the agents having fairly well-known safe threshold doses below which effects are assumed zero, ionising radiation exposure have no known safe threshold, low ionising radiation dose included. This leads to importance in of incorporating radiation protection measures in each such study protocol [1,18].

The ICRP 103 Recommendations [20] make it important to consider protection of research participants, facility radiation workers, also the public. These are considered under the three main components of justification, optimisation and dose limitation measures, well described by Martin and his group [1].

Regarding justification, there must be explanations supporting arguments for net benefit, needing to show that receipt of the radiation exposure outweighs potential harmful reactions and stochastic effects. The rationale for use of ionising radiation, without specific accompanying clinical use/indication must be discouraged and better

still, disallowed. Where there are accompanying clinical indications for the radiation, the number of exposures must be guided by what is appropriate for clinical use, not by the research. The clinical need for any exposure and accompanying radiation dose must be estimated, realising that the potential cumulative effect of exposures carries increased risk [18,21,22]. In such respect, several ionising radiation articles in Dentomaxillofacial Radiology were commented upon in a 2013 editorial to the journal, one notably on the number of radiation exposures in a particular study, more than expected for the clinical use and as stated in the protocol [23].

As part of exposure dose optimisation, the number of participants must be limited to the minimum number required to meet the objectives of the study. Dose constrains must be employed by ensuring that none of the participants are also involved in ionising radiation exposure from other sources. Moreover, the principle of ALARA (As Low as Reasonably Achievable) must be employed. This is achieved by minimising the exposure time, where possible maximising distance from the source of exposure, maximising shielding of exposed areas, and minimising the quantity of radiation from the source [9].

Efforts must be made to limit the exposure to a limited relevant area by coning. Where critical organs lie close to the field of interest, the organ area must be shielded. The radiation generated from the source must not be more than that required for the purpose. Where fluoroscopy is involved, the operator must be mindful of potential tissue harmful reactions [15].

Workers in the ionising radiation study facility must also be protected and monitored to ensure that their exposures remain below 20 mSv per year (and < 100 mSv per five years). Members of the public (e.g. anyone accompanying participants) must be kept away from the study ionising radiation to ensure that dose incurred is limited to below 1 mSv per year [1,24,25].

To avoid accidental radiation during pregnancy, the 10-day rule must be observed (women of childbearing age must not be exposed to ionising radiation after the first 10 days from the beginning of menstruation). When it is necessary to expose a woman of child bearing age and the menstrual dates are uncertain, the pregnancy test (blood hCG) must be negative. For radiation protection reasons it is best to avoid exposure during pregnancy [3,18,26,27].

Consent Process

In IR, the information provided about impact (especially when quantitative) is usually statistically derived, with associated uncertainty. This in turn affects the choice of language and efforts to ensure that research participants actually have a full understanding of the information [5,12]. The willingness of any study individual to take part in a study must be preceded by provision of a detailed study Participant Information Sheet (PIS). To ensure that the PIS are understood by the participant, it must be written in very simple language, devoid of medical terminologies. Any unavoidable terminology must be fully explained [28]. Ideally, the study investigator or a professionally capable delegate of the study investigator must also fully explain the PIS to the participant. The contents of the PIS must include statements of voluntariness of consent, details of the study, duration, and number of participants, risks and plans to communicate findings after the study [5].

The main area of challenge is the accuracy of the assessment of radiation risk. This is because there are no empirically derived radiation risk figures. Protection of individuals participating in radiation research requires the consideration of all potential risks relating to ionising radiation. The available quoted risks are derived from statistic probabilities [8,28,29]. Accordingly, there is a considerable degree of uncertainty in the risk information provided to participants concerning radiation exposure. As a result of the uncertainties, there is no clear agreement on the nature and contents of information to be provided to participants.

The random nature of the effect of ionising radiation creates difficulty when trying to be specific on known effects of IR, low dose effects overwhelmingly being stochastic (i.e. random and probabilistic). In practice, the stochastic risks of IR exposures are difficult to demonstrate using empirical data, the risks being based on calculations and extrapolation from epidemiological data. Cumulative effects and radio sensitivity in women are greater than in men and for children they are more than for adults. The cumulative dose effects and individual sensitivity to radiation exposure are modifying factors in radiation risk estimation. This is compounded by the degree of risk that is socially accepted despite the potential harm. On balance, writing appropriate PIS is at the best highly challenging. The consent process in terms of description of possible effects and degree of likelihood are important but difficult to be ascertained with as mentioned there being no generally acceptable and consistent quantitative data. The sentences must be carefully constructed, not just in simplicity of the language but in the expression of the contents, to improve the understanding of the risk [28,30].

Participant's right must be respected. Scrutiny is affected by expertise of the ethics committee. It is essential, that no such study must be carried out without gaining favourable

opinion/approval of an ethics committee. The study protocol must be detailed and be fully assessed by an ethics committee with advice from a clinical radiologist. The protocol must be scrutinised for input on radiation protection measures, where appropriate with pregnancy avoidance measures, ALARA exposures, immunological status, co-morbidity, and shielding of sensitive organs where possible.

Conclusion and Recommendations

This write up covers biological effects of radiation and the peculiar risks in various clinical categories such as pregnancy, paediatrics, apparently healthy adults and immunocompromised individuals.

The use of ionising radiation in clinical research requires understanding of the biological effects of radiation and peculiarities of the various clinical settings [9]. The quantitative uncertainties of radiation effects are a strong reason why it is important to avoid direct experimentation with ionising radiation.

Research is possible in scenarios where participants have simultaneous clinical diagnostic indications for radiation use; in such situations, unnecessary exposures to aid the research must be avoided. When research with IR is required, the ways of reducing risks are also to be discussed as a component of the research ethics assessment.

As part of the routine research ethics review, the dose resulting from IR on participants must be estimated. Knowledge of the vulnerability of the participant population, relevant organs and tissues must also be taken into account. In all cases, it is important for Clinical Radiologists to assess any need for exposure of participants and the Health Physicist to estimate radiation doses prior to commencement of the study. To achieve the best assessment, every review must involve appropriate experts (Clinical Radiologists and Medical Physicists) to secure opinions on the IR risk.

References

1. Martin A, Harbison S, Beach K, Cole P (2019) An introduction to radiation protection 7th (Edn.), CRC Press.

2. Lips M, Anderson E, Nakamura T, Harris F, Schneider G, et al. (2021) Reflections on low-dose radiation, the misconceptions, reality and moving forward. J Rad Prot 41: S306-S316.

3. Applegate KE, Findlay U, Fraser L, Kinsella Y, Ainsbury L, et al. (2021) Radiation exposures in pregnancy, health effects and risk to the embryo/foetus-information to inform the medical management of the pregnant patient. J Radiol Prot 41(4).

4. Brenner D, Elliston C, Hall E, Berdon W (2001) Estimated risks of radiation-induced fatal cancer from paediatric CT. AJR Am J Roentgeno 176(2): 289-296.

5. Nelson G, Anderson T, Nesovic L (2016) Low dose ionising radiation modulates immune function. Final Technical Report, pp: 1-36.

6. Lumniczky K, Candeias SM, Gaipl US, Frey B (2018) Editorial: Radiation and immune system: current knowledge and future perspectives. Front Immunol 8: 1933.

7. Lumniczky K, Impens N, Armengol G, Candeias S, Georgakilas AG, et al. (2021) Editorial: Low dose ionising radiation effects on the immune system. Environment International 149: 106212.

8. Classic KL, Porter BL, DiMagno EP (2001) Protection of research subjects with emphasis on protocols involving radiation. Health Phys 80: S70-S76.

9. Christensen DM, Iddins CJ, Sugarman SL (2014) Ionising radiation injuries and illnesses. Emerg Med Clin N Ame 32(1): 245-265.

10. Berrington A, Darby SC, Weiss HA, Doll R (2001) 100 years of observation on British Radiologists: mortality from cancer and other causes 1897-1997. Br J Radiol 74(882): 507-519.

11. Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, et al. (2007) The 15 country collaborative study of cancer risk among radiation workers in nuclear industry: estimates of radiation related cancer risks. Radiation Res 167(4): 396-379.

12. Mayo JR (2008) Radiation dose issues in longitudinal studies involving computed tomography. Proc Am Thoracic Soc 15(5): 934-939.

13. Strzelcyk JJ, Damilakis J, Marx MV, Madura KJ (2007) Facts and controversies about radiation exposure, Part 2: Low level exposures and cancer risk. J Am Coll Radiol 4(1): 32-39.

14. McBain-Miller J, Scurrah KJ, Brady Z, Mathews JD (2022) Cohort profile: The Australian paediatric exposure to radiation cohort (Aust-PERC). PloS ONE 17(9): e0271918.

15. Balter S, Miller D (2013) Patient skin reactions from interventional fluoroscopy procedures. AJR 202: W335-W342.

16. Wall B, Haylock R, Janson J, Hillier MC, Hart D, et al. (2011) Radiation risks from medical X-ray examinations as a function of the age and sex of the patients. HPA-CRCE.

17. Milner E (2006) Female breast radiation exposure. AJR Am J Roentgenol 186(6): E24.

18. Karoussou AS (2008) A preliminary study of issues and practices concerning pregnancy and ionising radiation. Radiation Protection Dosimetry 135(2): 79-82.

19. Bochud F, Cantone MC, Applegate K, Coffey M, Damilakis J, et al. (2020) Ethics aspects of radiation in medicine: update from ICRP Task group 109. ICRP Proceedings 49(1).

20. (2007) The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Annl ICRP 37(2-4): 1-332.

21. Karoussou AS (2008) Review of existing issues, ethics and practices in general medical research and in radiation protection research. Radiation Protection Dosimetry 129(1-3): 303-305.

22. Martin CJ, Barnard M (2022) How much should we be concerned about cumulative effective doses in medical imaging? J Radiol Prot 42(1).

23. Schulze R (2013) Editorial: Radiation protection vs research interests. Dentomaxillofac Radiol 42(2): 20120348.

24. European Commission Radiation protection 99 (1998) Guidance on medical exposures in medical and biomedical research. Luxembuurg: Offive for Official publications of the European Communities, pp: 1-24.

25. Faulkner K (2005) Personnel and patient doses: are there ethical consequences to the use of X-ray? Radiation Prot Dosimeter 117(1-3): 30-33.

26. European Commission Radiation protection 100 (1999) Guidance for protection of unborn children and infants due to parental medical exposure. Office for Official publications of the European Communities, pp: 1-40.

27. Karoussou AS (2009) A preliminary study of issues and practices concerning pregnancy and ionising radiation. Radiation Protection Dosimetry 135(2): 79-82.

28. Caon M (2008) Radiation information and informed consent for clinical trials. J Radiol Prot 28(3): 415-422.

29. Doudenkova V, Pipon JCB (2016) Duty to inform and informed consent in diagnostic radiology: How ethics and law can better guide practice. HEC Forum 28(1): 75-94.

30. Perko T, Raskob W, Jourdain JR (2016) Improved Communication, understanding of risk perception and ethics related to ionising radiation. J Radiol Prot 36(2): E15-E22.