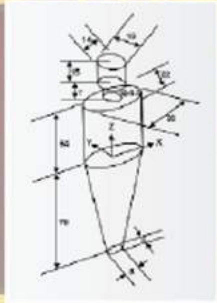

Dosimetry of Internal Emitters in Nuclear Medicine and Radiation Protection

AR Reddy & SC Jain

$$\bar{D}(v \leftarrow r) = k \frac{\tilde{A}_r}{m_v} \sum y_i E_i \phi_v (v \leftarrow r)$$

Defence Research & Development Organisation
Ministry of Defence, India

DOSIMETRY OF INTERNAL EMITTERS

DOSIMETRY OF INTERNAL EMITTERS IN NUCLEAR MEDICINE AND RADIATION PROTECTION

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From left to right: Top - PET, MIRD Phantom; Bottom - MIRD Equation, Indian Reference Male Phantom

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Foreword

As a former member of the Task Group of the ICRP on absorbed dose to patients from radiopharmaceuticals, which prepared in 1987 Publication no. 53, i.e., about 5 years after the first compilation of internal dose for administration of radiopharmaceuticals to patients in 1971, and Chairman of Committee-II of ICRP for several years, I wish to congratulate Alla R Reddy and Sheel C Jain for the present Monograph on Dosimetry of Internal Emitters in Nuclear Medicine and Radiation Protection.

After publication of a first full chapter on internal dosimetry by R. Loevinger, L.G. Holt, and G.J. Hine in 1956 in the famous book on Radiation Dosimetry, edited by G.J. Hine and G.L. Brownell, the MIRD Pamphlet 1 of the *Journal of Nuclear Medicine* in the 1960's, and the series of publications of the ICRP on dose to patients from radiopharmaceuticals from 1971 (Publ. 17), 1987 (Publ. 53), 1991 (Publ. 62), 1998 (Publ. 80) and most recently, of 2008 (Publ. 106), the present Monograph is a comprehensive and handbook-like publication on basic and practical internal dosimetry. It is useful for both medical physicists and nuclear medical physicians, either already working or while in education at medical schools or universities.

Both authors have already made important contributions in the past and this time also are going to make important contributions to the field of internal dosimetry in nuclear medicine and radiological protection. Personally, I am proud to have had the privilege and chance to work with Alla Reddy while he was working in my former Department for Biophysics and Radiological Protection at the Klinikum Steglitz of the Free University, Berlin, in 1975/76, and later, in 1983/84 in my Institute of Radiation Hygiene, in Munich, as an Alexander von Humboldt Senior Fellow. Apart from several common publications, Alla Reddy and I together published in 1989 a fundamental report on the question of "Dosimetry of Internal Emitters: At What Level?"

Our common international work on internal dosimetry was done in Committee-II of ICRP from 1993 to 2000 when I was Chairman of that Committee. Alla Reddy was engaged at that time in formulations of the Indian Reference Man in Jodhpur which was based on the work of Sheel Jain at INMAS on this subject.

Again, I may congratulate both authors for the excellent Monograph on medical dosimetry on internal emitters and may express my pleasure that I had the chance to work at least temporarily with Alla Reddy and to profit indirectly by the work done by Sheel Jain in internal dosimetry.

Alexander Kaul

Wolfenbüttel, Germany, May 2011

Preface

Dosimetry of internal emitters has a history of more than 60 years. It was initiated by Marinelli in the form of a research paper in 1942 giving out first formulae to estimate the dose due to internal emitters. The dose was expressed in the units of g-rad per mg-h in Marinelli-Quimby-Hine formalism for dosimetry of internal emitters in 1948, very similar to the unit used in radium usage for brachytherapy. Later, the unit evolved into g-rad per mCi-h initially in the Loevinger-Berman formalism for Medical Internal Radiation Dose (MIRD) Committee of Society of Nuclear Medicine, USA, when absorbed fraction was used for dose estimation in 1968, and then, while using specific absorbed fraction and SI units, the unit for absorbed dose was changed to $GyBq^{-1}s^{-1}$. When the absorbed dose is expressed as dose equivalent for organ dose estimates, considering biological effectiveness of different types of radiations using the radiation weighting factors, the unit used is $SvBq^{-1}s^{-1}$. Similarly for risk estimates due to internal emitters the parameter used is effective dose and the unit is $SvBq^{-1}s^{-1}$.

Loevinger-Holt-Hine wrote a full chapter on dosimetry of internally-administered radionuclides in the classic book on Radiation Dosimetry, edited by Hine and Brownell in 1956 based on the Marinelli-Quimby-Hine formalism with many illustrative examples of different radionuclides used in medicine. Nearly a decade afterwards, the Loevinger-Berman formalism for dosimetry of internal emitters came into vogue in the form of MIRD Pamphlet 1 in Supplement 1 of *Journal of Nuclear Medicine* based on absorbed fraction and specific absorbed fractions. A MIRD primer on this formalism was brought out by the Society of Nuclear Medicine, USA, in 1980s. Committee-II of the International Commission on Radiological Protection (ICRP) has its main task of the dose estimates due to internal emitters and it has brought out many of its reports on different aspects of dosimetry of internal emitters published as ICRP Publications in *Annals of ICRP* by Elsevier. Society of Nuclear Medicine, through its MIRD Committee, brought out many pamphlets on different aspects of dosimetry of internal emitters in nuclear medicine and also dose estimate reports for different nuclear medicine investigations with different radiopharmaceuticals. In 1989, a comprehensive report on Dosimetry of Internal Emitters: At What Level? was brought out by Reddy, Roedler and Kaul as ISH-HEFT 137 from Institute für Strahlen Hygiene, Munchen. Recently, Habib Zaidi and Sgouros have edited a book on Therapeutic Applications of Monte Carlo Calculations in Nuclear Medicine which has been published by the Institute of Physics, as part of its series on Medical Physics and Biomedical Engineering, in 2003. In 2008, Sgouros, Eckerman and Stabin brought out a book on dosimetric phantoms as part of the above series on Medical Physics and Biomedical Engineering.

This is the background with which we have undertaken to write the present monograph on ‘Dosimetry of Internal Emitters in Nuclear Medicine and Radiation Protection’ as part of the Monographs/Special Publications Series of Defence R&D

Organisation (DRDO) of Ministry of Defence, Government of India. The Monograph has 8 chapters and number of sections and sub-sections in each chapter on different aspects of the dosimetry of internal emitters. Chapter 1 is an overview of the subject for first-pass reading and rest of the 7 chapters deal with the subject in greater detail. The two major formalisms, viz., Marinelli-Quimby-Hine formalism and Loevinger-Berman formalism for dose estimations due to internal radionuclides used by MIRD and ICRP have been described in Chapter 2. Dosimetric concepts and quantities are the subject matter for Chapter 2. Physical and biological information inputs required for dose estimation are the subjects dealt with in Chapters 3 and 4, respectively. Stylised phantoms for ICRP Reference persons and for proposed Indian Reference Adult including their mathematical description is described in the Chapter 5 titled Dosimetric phantoms. Description of the voxel phantoms for ICRP Reference Adult is also included in this chapter. Monte Carlo computational techniques for estimation of absorbed dose due to internal radionuclides is the topic of Chapter 6. Dose estimations due to internally-administered radionuclides in normal practices of diagnosis and therapy in nuclear medicine and in radiation safety are dealt in Chapter 7. This chapter includes many examples of targeted radionuclide therapy regimes with emphasis on dose estimation and issues of radiation safety in these practices. Embryo-foetus dosimetry and dose estimations for Indian Adults have also been included. At what level the dosimetry of internal emitters is to be carried out and uncertainties in such absorbed dose estimations have also been dealt in Chapter 7. Dose reconstruction and retrospective dose estimation, decontamination and decorporation in radiation emergencies are briefly dealt in Chapter 8. *Appendix A* lists all the MIRD Pamphlets and MIRD Dose Estimate Reports and *Appendix B* lists all the ICRP Publications brought out until 2008.

We expect the Monograph to be useful for the physicians, physicists, technologists working in nuclear medicine institutions and to those involved in radiological safety.

In preparing this Monograph, we have extensively used material from many research publications, MIRD Pamphlets, ICRP Publications. We have referred to such materials at appropriate places in the text and in the list of references at the end of each chapter. Many cited references, particularly those on formalisms, standardisation, and harmonisation of dosimetry of internal emitters and targeted radionuclide therapies are from the *Journal of Nuclear Medicine*, USA, and those on ICRP Biokinetic Models and ICRP Recommendations are from the ICRP Publications from *Annals of ICRP*. We gratefully acknowledge the benefits that have resulted from them. The chapter on Monte Carlo computational techniques with many examples of computations was written by Dr Ayyangar Komanduri, Former Professor of Medical Physics in University of Nebraska, Oklahoma, USA, as personal communication and we are indebted to him for the help. Some figures and tables have been reproduced with specific permissions from the authors and publishers. We gratefully acknowledge the prompt permission given by both the authors and the publishers.

We are indebted to Dr AR Sundararajan, Former Head, Radiation Safety Division, Atomic Energy Regulatory Board, Mumbai, and Prof GS Pant, Former Professor, Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, for providing valuable inputs in the preparation of this Monograph. We express our thanks to Prof. Alexander Kaul, Former Chairman, Committee 2, ICRP, for his encouragement and nice Forward to the Monograph. One of the authors (ARR) had the previlege of closely working with him as Alexander von Humboldt Senior Research Fellow. We appreciate the helpful comments on the Monograph by Shri PK Bhatnagar, Associate Director (retired), Defence Laboratory, Jodhpur.

We thank the authorities of Defence Research & Development Organisation (DRDO) for sanctioning a Project to us to write this Monograph through Defence Scientific Information and Documentation Centre (DESIDOC) as part of their Monographs/Special Publications Series. Dr W Selvamurthy, Chief Controller R&D (Life Sciences & International Cooperate), DRDO, encouraged us and gave valuable suggestions in writing this Monograph. He has also kindly written the Foreword for this Monograph. We gratefully acknowledge his kind help and encouragement. Dr AL Moorthy, Director, DESIDOC, Ms Alka Bansal, and editorial team have provided valuable technical support in the preparation of this Monograph and we acknowledge their kind help. Directors of Defence Laboratory, Jodhpur, and Institute of Nuclear Medicine & Allied Sciences, Delhi, have been kind enough to permit us to use their library resources and we gratefully acknowledge their support.

Last but not the least, we express our appreciation to our spouses Smt A Indira Reddy and Smt Sheela Jain for their patience and understanding in putting up with us during the many months of our involvement in writing this Monograph.

Hyderabad — AR Reddy
Delhi — SC Jain

Contents

Chapter 1

Dosimetry of Internal Emitters: An Overview

1.1 INTRODUCTION

Radionuclides occur naturally and are also man made in reactors, with accelerators and from radionuclide generators. They exist in environment, biota, and human beings. Uranium and thorium series constituting radioactive substances and ^{40}K are part of terrestrial natural environment. ^{14}C, ^{137}Cs, ^{90}Sr are examples of atmospheric nuclear tests and are seen also in biota and human beings. Radioactive substances like ^{131}I, ^{99m}Tc, and many others, tagged to pharmaceuticals are used in nuclear medicine for both diagnostic and therapeutic purposes. ^{60}Co, ^{192}Ir, ^{137}Cs are used in radiotherapy. Radioactive substances are also used in industry, agriculture, and research. All the radioactive substances emit ionizing radiation. When the radionuclides are part of a biological system, either administered intentionally just as in nuclear medicine or taken up inadvertently from workplaces or from environment, they are termed internal emitters. Exposures to ionizing radiation from internal emitters are internal exposures. When the radioactive substances are part of the environment, external to human being, and if human beings are exposed to such radioactive substances, then they are termed external exposures. Physical parameter used to represent the radiation exposures is the absorbed dose.

Beneficial uses of both *x*-radiation and radioactive substances followed immediately after their discoveries. However, soon after, it was also realised that exposures to the ionizing radiation, either internally or externally, do result in harmful effects. Hence, while justifying the beneficial use of radiation or radioactive substances, it became imperative to assess the harm in terms of risks involved. Risk is a probabilistic quantity. It, due to exposures to ionizing radiation, is assumed to be linearly proportional to the amount of radiation exposure received and absorbed by the exposed individuals. Thus, any practice that uses ionizing radiation has not only become essential to be justified, its optimisation to ensure radiation exposure is kept to a minimum in such justified use has also become mandatory. Dose limits to radiation workers and members of public are prescribed as part of regulatory norms of any radiation safety program.

Dosimetry of internal emitters deals with the quantification of the amount of energy imparted to a target in a biological system due to different types of radiation emitted from a radionuclide distributed in it or elsewhere in the system. It is also concerned with the spatial and temporal distributions of this imparted radiation energy in the target. The target in nuclear medicine procedures or in radiation safety could be the whole body, or an organ, or a tissue, or a cell or a sub-cellular structure. Energy imparted to a target is converted to absorbed dose. Dose computations are done, not only in medicine but also for the purposes of radiation safety and other environmental issues.

The internal dose estimation requires basically two parameters. First one is a physical quantity, *S*-factor, given in unit, Sv Bq^{-1}. It encompasses age- and sex-specific Reference Person data representative of shape and size of relevant human body as well as its composition (dosimetric computational models) and radionuclide decay characteristics such as the type of radioactive decay, half-life, type and frequency of ionizing radiation emitted in the decay of the radionuclide. Computation of *S*-factor involves complex Monte Carlo calculations to get radiation energy absorbed in the biological target of interest in terms of either absorbed fractions or specific absorbed fractions. Second parameter is a biological quantity. Its estimation involves the use of bioassay methods to get information on biokinetics of the radionuclide in the biological target. The parameter estimated is the cumulated activity, $\tilde{A}$, in the unit Bq s. Thus, the estimated radiation absorbed dose is an important physicobiological parameter that is considered to be a reasonably good parameter to estimate the harm or risk due to ionizing radiation from the use of an internal radionuclide. It is also used for assessing the benefit versus risk due to use of internal administration of radionuclides, either in medicine or in other fields.

In the diagnostic use of a radionuclide, the associated risk to the patient due to radiation dose is insignificant compared to the diagnostic information derived for his/her benefit. Hence, estimation of an average dose assuming uniform distribution of radioactivity in the target organ, is considered sufficient. Number of medical internal radiation dose (MIRD) pamphlets giving basic methodology and tables of data required for dosimetry have been published. Using, as far as possible, human biokinetic data (for normal individuals), best estimates of the dose for several radiopharmaceuticals have been published. At this point it must be emphasised that all the physical data tabulated (like absorbed fractions or *S*-factors) so far are for specific mathematically defined models. Therefore, the dose estimates in the above MIRD pamphlets should be used as guidelines for general population, not for a specific individual or a patient.

However, when the activity distribution is examined at microlevel (for example distribution of radioiodine in thyroid follicle), or even at organ level sometimes (for example, distribution of radioiodine in human thyroid tissue when it is used for therapy of different thyroid diseases), many times there is non-uniformity in its distribution. If the particulate radiations emitted from the radionuclide are penetrating enough as compared to the linear dimensions of a defined target of interest, the dose distribution could still be uniform, and hence, the average dose estimate will be sufficient. But if the radiations emitted are of low energy with smaller range as compared to the target, the average dose estimate at an organ or at gross tissue level loses its meaning and dosimetry is to be done at a local level with the knowledge of microlocalisation as well as microdistribution of the radionuclide, its decay characteristics and range-energy or energy loss relationships. This has become essential in case of radionuclides that decay by electron capture and isometric transitions resulting in Auger electron emissions (whose ranges are nearer to the linear dimensions of the sub-cellular structures). With the increasing availability of means to obtain time-activity details for specific patients (that is availability of patient-specific biokinetics of the radiopharmaceutical) in nuclear

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About the Book

Monograph on Dosimetry of Internal Emitters in Nuclear Medicine and Radiation Protection provides in a comprehensive manner different aspects of the subject that would be useful to students, teachers, and researchers in nuclear medicine and radiological safety. The book starts with a crisp overview of the subject for the first pass reading. It covers basics such as dose concepts, radionuclide decay schemes, interaction of radiation with matter, essential physical as well as biological inputs for dose estimates, and ICRP recommendations. Advanced topics like dosimetric formalisms, dosimetric phantoms, Monte Carlo computational techniques for dose estimation, dosimetric aspects of targeted radionuclide therapies, embryo/fetus dosimetry, level of dosimetry of internal emitters relevant for different situations, and uncertainties in dose estimations have all been dealt in detail. Formulation of Reference Indian Adult and its mathematical description as well as dose estimations in different diagnostic nuclear medicine investigations applicable to Indian Reference Adults are also included. Dose reconstruction, retrospective dose estimation, and decontamination and decorporation of internal contaminations in cases of radiation emergencies have also been presented briefly.

About the Authors

Dr Alla Ramalinga Reddy obtained his PhD in 1965 from Andhra University and Post-doctoral research at Massachusetts General Hospital, Boston, USA under Prof GL Brownell from 1965-68 on different aspects of dosimetry of internally-administered radionuclides. He was consultant to Medical Internal Radiation Dose Committee of Society of Nuclear Medicine, USA (MIRD), to bring out in 1968, the MIRD Pamphlet No. 3 on 'Absorbed Fractions for Photon Dosimetry' as part of the Supplement 1 of *Journal of Nuclear Medicine*, 1968. He joined Institute of Nuclear Medicine & Allied Sciences (INMAS) and made important contributions in internal dosimetry with special reference to ^{125}I microdosimetry and embryo/fetus dosimetry. He was awarded the prestigious Alexander Von Humboldt Senior Fellowship by Institute of Radiation Biophysics, Berlin, Germany, from 1975-76 and by Institute of Radiation Hygiene, Munich, Germany, from 1983-84 in the field of internal dosimetry. He joined Defence Laboratory (DL), Jodhpur, and established a Radioisotopic Application Laboratory during 1980s and became Director, DL, Jodhpur in 1993. He moved to DRDO HQrs in 1997.

Dr Sheel Chand Jain obtained his PhD in 1983 from University of Delhi. He joined INMAS in 1967 and worked on whole body counters and body potassium measurements. He moved to Defence Institute of Physiological and Allied Sciences in 1972 to establish radiotracer facilities for measurement of a number of physiological functions under different environmental conditions including high altitude. He joined DL, Jodhpur, 1986-89 to work on NBC defence. In mid-1989, he moved to INMAS and worked on formulation of Indian Reference Man and estimation of radiation dose from administration of radiopharmaceuticals to Indian subjects. He also served Centre for Environment and Explosive Safety from 1996 to 2004. Presently, he is Vice-Dean of Indian College of Nuclear Medicine and a Central Council Member of IDST.

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