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Special Issue
Ionizing Radiation in Medicine

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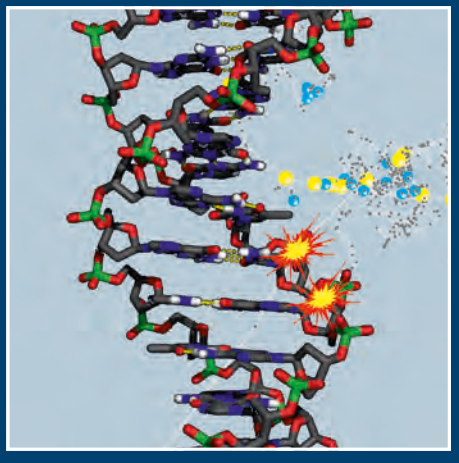

Physikalisch-Technische Bundesanstalt ■ Braunschweig and Berlin
National Metrology Institute

PTB mitteilungen

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Contents

Ionizing Radiation in Medicine

Cover picture:

How is ionizing radiation used in medicine and which radiation effects occur in this field? The articles in this issue of *PTB-Mitteilungen* answer these questions. The photos on the title page refer (from left to right) to the radiation effect on biological objects (see p. 72), to the activity determination of radionuclides (see p. 16), and to radiation protection in medicine (see p. 41).

Imprint

The *PTB-Mitteilungen* are the metrological specialist journal and the official information bulletin of the Physikalisch-Technische Bundesanstalt. As a specialist journal, the *PTB-Mitteilungen* publish original scientific contributions and general articles on metrological subjects from the areas of activities of the PTB. The individual volumes are focused on one subject. As the official journal, the *Mitteilungen* have a long tradition dating back to the beginnings of the Physikalisch-Technische Reichsanstalt (founded in 1887).

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Preface

Herbert Janßen*

The term "ionizing radiation" – often wrongly designated as "radioactive radiation" in everyday linguistic usage – regularly awakes very ambiguous feelings in all of us as "radiation" is commonly associated with a threat to life and one's physical well-being which is often not exactly quantifiable. Yet, each human being is subjected to ionizing radiation, in all places and at all times – this radiation mostly occurs naturally. We have already dedicated one of our previous issues to ionizing radiation in the environment and its influences on our social life (cf. PTB-Mitteilungen, Vol. 4.2006). The articles in this issue now deal with the applications of ionizing radiation in medical diagnostics and therapy. In contrast to the inevitable exposure due to natural radiation sources, the application of ionizing radiation to persons must always be medically justified, so that the benefits for the patients always outbalance the risks.

It is not incumbent on PTB to directly apply radiation to persons, and it is the attending physician's role to weigh the benefits and risks for the patient. But one of the essential aspects which has to be considered for all decisions having to do with the use of ionizing radiation is the measurement of the physical quantities that are relevant for diagnosis and therapy, which has to be as accurate and, in particular, as correct as possible. The relevant measurands are, for example, the activity of radioactive substances, measured in becquerel, or the dose when it comes to the therapy applied to treat tumours with diverse radiation qualities, measured as the absorbed dose to water in gray. But this also includes the reliable determination of radiation doses, measured in sievert, which the staff in medical surgeries and hospitals may be exposed to in their daily work routine.

The following contributions of PTB colleagues from the "Ionizing Radiation" Division deal with such metrological topics with regard to the use of ionizing radiation in medicine. The objective was not to describe individual diagnostic or therapeutic procedures from the field of medical engineering which has experienced a fast-paced development. The focus lies on the metrological bases and procedures used for the transfer between the realization at the national metrology institute (PTB) and the respective medical application of the measurands that are important in medicine, which is done, as far as possible, in a practice-oriented way.

After a short introduction into the utilization of ionizing radiation in diagnostics and therapy, we will deal with dosimetry in X-ray diagnostics. After that, the procedures which are used to determine the activity of radioactive sources and to measure the dose of special radioactive sources used in brachytherapy will be introduced. The basic measurand for the treatment of tumours with ionizing radiation is the absorbed dose to water. The measurement method developed at PTB for the absolute determination – water calorimetry – will be presented, as well as the relative measurement procedure for medical practice which is based on ionization chambers and alanine.

Radiation protection for medical staff and, if necessary, for assisting persons is an important aspect that will be examined closely. Contrary to the patient, for whom the dose is justified by medical indication, the dose to which the staff is exposed due to their occupation must obviously be kept as low as possible. For this group of persons, dose limits have been laid down and compliance with these must be monitored by means of appropriate dosemeters. The following articles will report on the measurands used in radiation protection, on measuring instruments, on the system of official personal dosimetry as well as on the particular metrological challenges for dosimetry that arise from the use of pulsed radiation sources.

The dose measurands currently used for diagnostics and therapy as well as for radiation protec-

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tion are defined macroscopically. We consider the mean energy of the penetrating radiation which is deposited in a larger volume and use the empirical radiation and tissue weighting factors in radiation protection to take the different biological effectiveness levels of various radiation qualities in different organs and tissue into account. PTB's work on the microscopic effect of ionizing radiation on bio-molecules and cells as well as their simulation in numerical models will be presented in the concluding articles of this issue.

Ionizing Radiation in Diagnostics and Therapy

Ulrike Ankerhold*

Introduction

Ionizing radiation is not visible and cannot be perceived with the senses which humans have such as, e.g., the sense of smell or the sense of hearing. Exposure to ionizing radiation can damage people's health and lead to serious diseases. On the other hand, ionizing radiation has become an indispensable tool of modern medicine. At the right dose, it is used in diagnostics and in radiation therapy for the patient's good, either to detect diseases and decide upon the treatment, or for the targeted destruction of tumours.

In medicine, imaging diagnostic methods such as MRI, ultrasound, endoscopy and X-ray diagnostics (as the one most frequently used) are applied. In hospitals, X-ray radiation is used for approx. 63 % of the imaging diagnostics (see Fig. 1).

Special radionuclides having particularly well-suited decay properties are used to complement the traditional imaging methods based on X-rays which penetrate the body from the outside. The patients are administered these radionuclides in the form of a radiopharmaceutical. By selecting the appropriate chemical compound, the radionuclides gather in certain organs or tissues of the body. The radiation properties of the atoms decaying inside the body are then exploited for imaging, e.g. by means of gamma cameras or positron emission tomography (PET).

In radiation therapy, the damaging effect of ionizing radiation is exploited to kill cancerous cells; this effect depends on the dose applied. At approx. 25 %, cancer is one of the most frequent causes of death in the industrialized countries. 50 % to 60 % of all cancer patients are treated by means of radiation therapy within the course of their treatment; in approx. 50 % of all long-term tumour cures, it is one of the components of therapy or sometimes even the only treatment

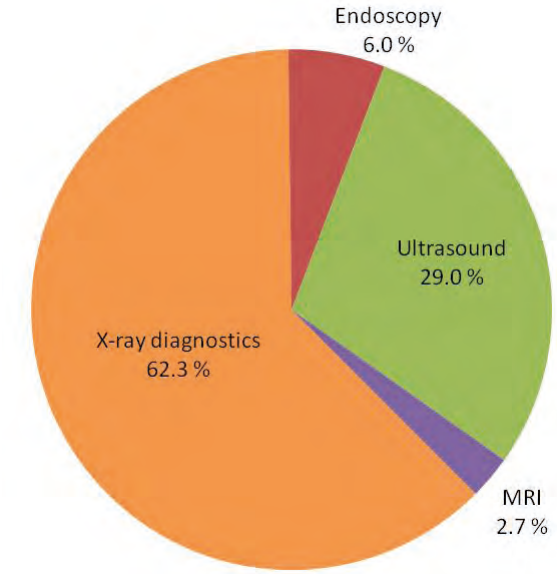

Fig. 1: Frequency of use of different methods in imaging medical diagnostics in hospitals.[1]

method[2].

In radiation therapy, one differentiates (apart from interoperative irradiations) between external radiation therapy and internal radiation therapy – the latter being called "brachytherapy". In *external radiation therapy*, the patient (or rather the tumour) is irradiated from outside the body. Hereby, it is unavoidable that the healthy tissue above the tumour is also exposed to radiation along with the tumour which is located somewhat deeper. In routine clinical practice, external radiation therapy is performed with high-energy photon radiation (which is generated by clinical electron linacs) due to its greater penetration depth. All developments in radiation therapy are aimed at attaining a sufficiently high and uniformly distributed dose in the tumour while only applying a small dose to the healthy tissue surrounding the tumour in order to prevent damage. The key term is "tumour-matched dose

[1] BMU-2005-660: *Erfassung der Häufigkeit bildgebender Diagnostik, insbesondere strahlendiagnostischer Massnahmen und der Altersverteilung der Patienten,* Schriftenreihe Reaktorsicherheit und Strahlenschutz, Bundesministerium für Umwelt und Reaktorsicherheit, 2005

[2] Die blauen Ratgeber: Strahlentherapie, Antworten, Hilfen, Perspektiven, Band 53, Deutsche Krebshilfe e.V.

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distribution". One of the latest developments in external radiation therapy is Intensity Modulated Radiation Therapy (IMRT), where the patient is irradiated from different directions by means of a large number of narrow radiation fields that have irregular shapes and are adapted to the tumour's geometry.

In *brachytherapy*, in contrast, the tumour is irradiated directly by inserting small radioactive sources into the patient which are placed inside the tumour or close to it. The great advantage of this form of therapy is that healthy tissue located away from the tumour is not irradiated. Modern brachytherapy mainly uses radioactive photon radiation sources – either high-dose-rate sources (e.g. Ir-192 sources) or low-dose-rate sources (e.g. I-125 seeds), depending on the type, geometry and position of the tumour in the body. By using several seeds at the same time or one HDR source and changing its position, one attains a uniform and sufficiently high dose distribution in the tumour. In this form of therapy, too, it is unavoidable that healthy tissue in the direct vicinity of the tumour is irradiated. In order to protect radiation-sensitive tissue close to the tumour, so-called applicators with the most varied geometries are used to shield sensitive organs from the radiation field. One of the latest developments in brachytherapy is the use of miniaturized X-ray facilities. Instead of using radioactive sources, whose handling requires sophisticated radioprotection measures, therapy is performed with smallest X-ray tubes (tube voltages up to 50 kV) which are introduced directly into the body. With this method, too, the geometry of the radiation field inside the patient is adjusted by means of applicators.

When using ionizing radiation in medicine, the dose and its uncertainty are very important. The so-called "ALARA" principle applies meaning "as low as reasonably achievable". In diagnostics, the challenge resides in applying a dose to the patient which will be as small as possible, but high enough to obtain meaningful imaging – and thus, a reliable diagnosis. In radiation therapy, the dose deposited in the tumour has to be high enough to kill cancerous cells, but at the same time, the dose should not be too high in order not to cause unnecessary damage to the surrounding healthy tissue. To summarize: for the patient's good, reliable and traceable dosimetry with a correspondingly low measurement uncertainty – and whose quality assurance is guaranteed – is of paramount importance both in diagnostics and in radiation therapy. Report 24 by ICRU (International Commission of Radiation Units and Measurements)[3] requires, for optimum radiation therapy, that the uncertainty of the dose deposited in the tumour be no more than +/- 2.5 % (k = 1). In X-ray diagnostics, Report 74 of ICRU[4] requests a total uncertainty of the dose measurement of 7 % (k = 2). Today, these two requirements are, unfortunately, not always attained; especially in radiation therapy, measurement uncertainty still represents a huge challenge. In radiation therapy, the dose measurand is the absorbed dose to water, in X-ray diagnostics, the base measurand of dosimetry is the air kerma. Both measurands are expressed in the unit "gray" (abbreviated to "Gy"; Gy = J/kg).

For the realization of the units of these measurands, PTB operates various primary standards (see the articles "Calorimetric Determination of the Absorbed Dose to Water", "Dosimetry for Brachytherapy" and "Metrological Aspects of Dosimetry in X-ray Diagnostics" in this publication). Through the calibration of secondary standards, the units are disseminated and traceability in dosimetry is, thus, ensured. In X-ray diagnostics, the use of dosimeters having a type-approval certificate is prescribed by the quality-assurance requirements for certain measurement applications. In the field of dosimetry in radiation therapy, the regulations of the Medical Devices Act and of the Medical Devices Operator Ordinance apply.

The secondary standards used in X-ray diagnostics and radiation therapy are nearly exclusively ionization chambers (see the article "Dosimetry with Ionization Chambers in External Radiation Therapy" in this publication). These exhibit high metrological stability and reliability, good measuring characteristics (e.g. low energy dependence of the response), and their properties are easy to describe by means of numerical simulations. Ionization chambers of the most differing shapes (cylindrical, spherical or flat and coplanar chambers) and air volumes (volumes from 0.015 cm^3 to 0.6 cm^3 in radiation therapy and up to approx. 100 cm^3 in X-ray diagnostics) are used, depending on the requirements of the measurement.

Besides direct dose measurement, radiation transport calculations based on Monte Carlo simulations are an important tool to determine dose values, dose distributions, correction factors, the response of detectors, etc. Such calculations can be used, on the one hand, to understand measurement results and draw the correct conclusions from them, and, on the other hand, to determine parameters which cannot be determined by means of measurements. Radiation transport calculations must categorically be considered as a complement to measurements.

The technical developments in radiation therapy and X-ray diagnostics keep presenting dosimetry with new challenges. Examples are – in radiation therapy – dose measurement in small fields and – in X-ray diagnostics – dosimetry in the broad radiation field of modern CT devices. Research and development activities for new detectors,

[3] International Commission on Radiation Units and Measurements, *Determination of Absorbed Dose in a Patient Irradiated by Beams of X or Gamma Rays in Radiotherapy Procedures*, ICRU Report 24, 1991

[4] International Commission on Radiation Units and Measurements, *Patient Dosimetry for X-rays used in Medical Imaging*, ICRU Report 74, Journal of the ICRU, Vol. 5, No. 2 (2005), Oxford University Press

measurement procedures, etc. play an important role in realizing traceable dosimetry in these novel fields. Due to the small size, to the low dependence of the response on the radiation quality and to the material properties, the alanine dosimeter is an essential piece of measuring equipment for such investigations (see the article "Alanine Dosimetry" in this publication). There is close national and international cooperation between medical physicists in hospitals and experts from other national metrology institutes, calibration laboratories, and industry. PTB transposes the research results into national and international standardization as well as into internationally applied technical documents (e.g. IAEA Reports).

Metrological Aspects of Dosimetry in X-ray Diagnostics

Ludwig Büermann*

1 Introduction

In 2010, the average effective dose per person and year caused by ionizing radiation from natural and artificial sources amounted to 3.9 mSv in Germany. Nearly half of this amount, i.e. approx. 1.7 mSv, originated from X-ray examinations [1]. These numbers make clear how important dosimetry is for quality assurance in X-ray diagnostics and how important it is, thus, to achieve sufficient image quality with a minimum dose. What is also of interest are the percentages of the different types of X-ray-diagnostic examinations and the shares they have in the collective effective dose (see Figure 1). The collective dose is the product of the number of persons belonging to the exposed population group and the mean per capita dose. The unit of the collective dose is the *man sievert*. The term *effective dose in X-ray diagnostics* is described in more detail in section 6.

What is particularly striking is that although only 8 % of the X-ray examinations are carried out by means of computed tomography (CT), these represent 60 % of the collective effective dose. In turn, the share of dental examinations amounts to 42 %, causing, however, only 0.2 % of the dose. By means of statistical investigations of this kind, valuable conclusions can be drawn with regard to particularly high-dose or low-dose examinations. Also, those examination types become obvious where special attention must be paid to quality assurance. The frequency of X-ray-diagnostic examinations is monitored by the *Bundesamt für Strahlenschutz* (Federal Office for Radiation Protection – BfS) on behalf of the *Ministry for the Environment* (BMU) with the aid of the tariff numbers which are indicated in the bills of the health insurance companies. These are made available to the BfS by the cost-bearing associations (i.e. the *Association of Statutory Health Insurance Physicians*, the *German Dentists Association*, and the *Association of Private Health Insurance Providers*) [1]. In which way, however, are the effective patient doses determined? How is the quality of the medical X-ray equipment ensured? Which role does dosimetry play in X-ray diagnostics

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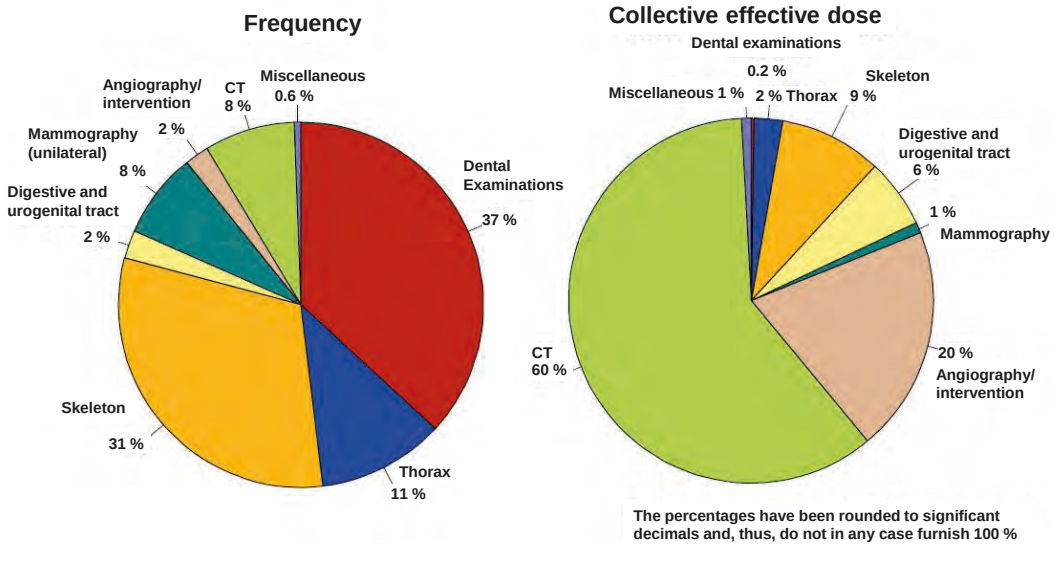

Figure 1: Percentage of the different types of examinations contributing to the overall frequency and to the collective effective dose in Germany in 2010 (source: [1]).

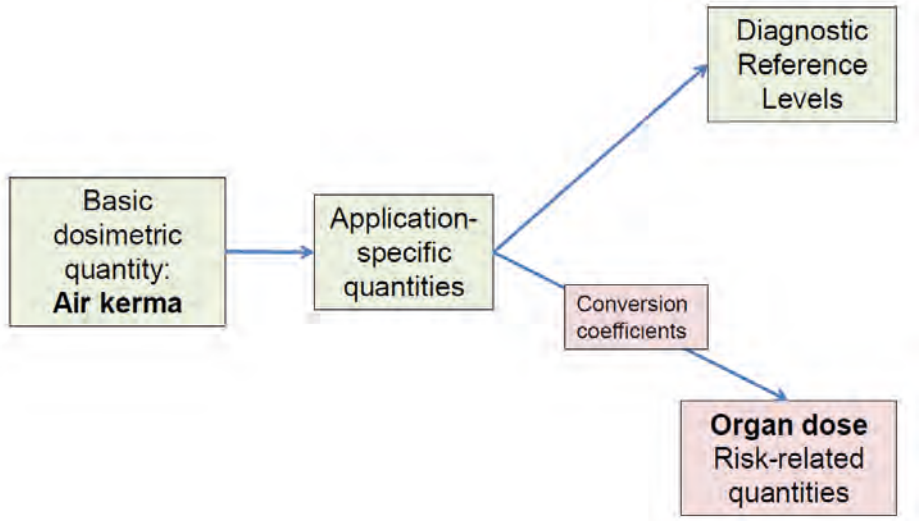

Figure 2: From the basic quantity "air kerma" via application-specific dose quantities to diagnostic reference values and effective patient doses.

and, thus, PTB? With which uncertainties should dosimetry be carried out? These questions will be answered in the following article.

2 From measurable dose quantities to the patient dose

The basic quantity in *dosimetry for X-ray diagnostics* is the air kerma, which is a fundamental quantity in photon dosimetry (see section 3). From the air kerma, the application-specific dose quantities for applications such as radiography and fluoroscopy (4.1), mammography (4.2) and computed tomography (4.3) are derived (section 4). Application-specific dose quantities provide the basis for quality assurance in X-ray diagnostics – for example, for acceptance and constancy testing, or for the diagnostic reference levels (see section 5). From the application-specific dose quantities, also the organ-absorbed dose and the tissue-absorbed dose (which are both not directly obtainable by means of measurements) and the effective dose for standard patients are determined, with the aid of calculated conversion factors (see section 6). According to a recommendation of the ICRU (International Commission on Radiation Units and Measurements), dose measurements for quality assurance and the determination of the patient dose should be carried out with an expanded uncertainty ($k = 2$) of less than 7 % [2]. This allows uncertainty requirements to be derived for the metrological chain of dose measurement – from the primary standard to application-specific dose quantities (see section 7).

3 Definition and primary measurement of the air kerma

The quantity "air kerma" originates from the idea that the transmission of energy to the medium "air" by X-rays is performed in two steps: first, electrons are released by photons interacting with the atoms of the air. Along their paths, the electrons transmit energy to the air by ionization and excitation. A fraction of the kinetic initial energy of the electrons is converted into bremsstrahlung and is not deposited locally in the vicinity of the electron paths. The first step of electron release is physically described by the quantity **kerma** (**k**inetic **e**nergy **r**eleased per unit **ma**ss) [3], the second by the absorbed dose to air. The air kerma of X-rays from conventional X-ray tubes is measured by means of free-air ionization chambers [4] which work according to the principle shown in Figure 3.

An – almost parallel – X-ray beam enters through a diaphragm (having the cross-sectional area A) into an air-filled, open parallel-plate chamber and leaves it through an outlet. The axis of the X-ray beam crosses in the centre of a plate pair whose upper plate (H) lies at a higher electrical potential than the lower plates (S-M-S). The electrical field between the plates serves to separate the ion pairs generated by the X-rays via secondary electrons. The charges are collected by the measuring electrode (M) whose length in beam direction defines the ion-collecting volume (V_I). The guard electrodes (S) serve to realize a homogeneous electrical field in the collecting volume. The dimensions of the chamber must be selected in such a way that secondary electron equilibrium (SEE) exists for the measuring volume (V_M, hatched area in Figure 3). Under SEE conditions, the absorbed dose to air corresponds to the air kerma, except for the bremsstrahlung losses. With the aid of the ionization constant for air ($W/e = 33.97$ J/C), the ionic charge measured by means of a free-air

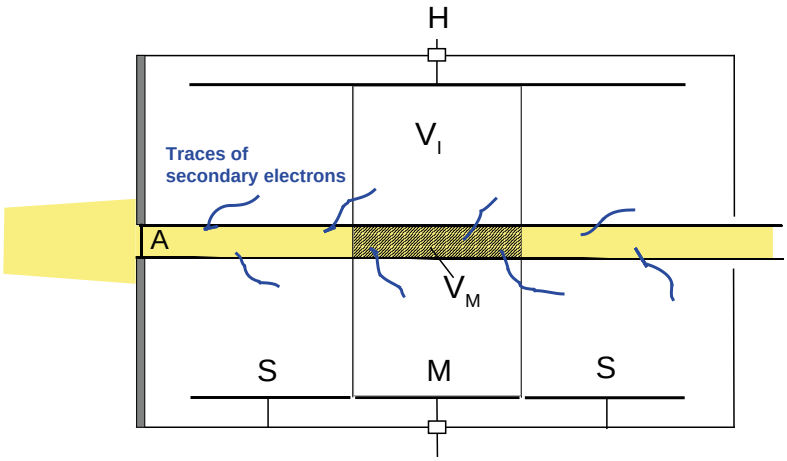

Figure 3: Measurement principle of a free-air chamber. A: cross-sectional area of the circular aperture, H: high-voltage electrode, S-M-S: opposite electrode, subdivided into guard electrodes (S) and measuring electrode (M), V_i: ion-collecting volume, V_M: measuring volume.

chamber under SEE conditions can be converted into the absorbed dose to air. Thereby, the following relation between the air kerma K_a and the specific charge Q/m ($m = \rho V_M$) is obtained:

$$K_a = \frac{Q}{m}\frac{W}{e} k_g \prod k_i$$

The deviations of a real free-air chamber from an ideal one are taken into account by the product of correction factors k_i. k_g is the correction factor for the bremsstrahlung losses. The unit of air kerma is the "gray" (Gy = J/kg). With the aid of free-air chambers, the air kerma of X-rays generated with tube voltages between 10 kV – 400 kV can be measured with an expanded ($k = 2$) relative uncertainty of about 0.6 %.

For the field of X-ray diagnostics, PTB operates two different free-air chambers: the parallel-plate chamber (referred to as "PK100"), and a cylindrical free-air chamber (referred to as "FK" ("Fasskammer")) (see Figure 4). The PK100 is used to calibrate secondary standards used in mammography (tube voltages: 25 kV to 35 kV), whereas the FK serves to calibrate standards used in conventional radiography (tube voltages: from 50 kV to 150 kV). The calibration factors of the secondary standards are indicated with relative expanded ($k = 2$) uncertainties of approx. 1 %. For the calibration, reference radiation fields (radiation qualities) as defined in the international standard IEC 61267 are used. The photon fluence spectra of all radiation qualities were measured with a high-purity germanium detector. Figure 5 shows examples of photon fluence spectra measured in mammography. The structure of the spectra shown can be explained by the prominent K-fluorescence radiations of the anodes (Mo and Rh) and the K edge filters of Rh and Mo. The spectra provide the basis for the calculation of mean correction factors for the free-air chambers and for the calculation of radiation quality parameters such as the mean energy or the half-value layer with respect to aluminium.

4 Application-specific dose quantities

All application-specific dose quantities are based on the air kerma. In the terminology of *dosimetry in X-ray diagnostics*, however, the general term "dose" is used although – strictly speaking – the quantity "air kerma" is meant. In the following, the term "dose" therefore always means "air kerma", unless the organ-absorbed dose or the effective dose are explicitly meant. A comprehensive survey of *dosimetry in X-ray diagnostics* is given in ICRU Report 74 [2].

4.1 Radiography and fluoroscopy

The typical beam path from the focus of the X-ray tube to the imaging system in classical projection radiography is represented schematically in Figure 6. Depending on the type of recording, tube voltages in the range from 60 kV to 120 kV, which are filtered with aluminium of different thicknesses, are used. X-ray tubes with rotating anodes of tungsten are used. Here, the most important quantity is the so-called "dose area product" (DAP) which is measured close to the focus with the aid of DAP measuring chambers. DAP mea-

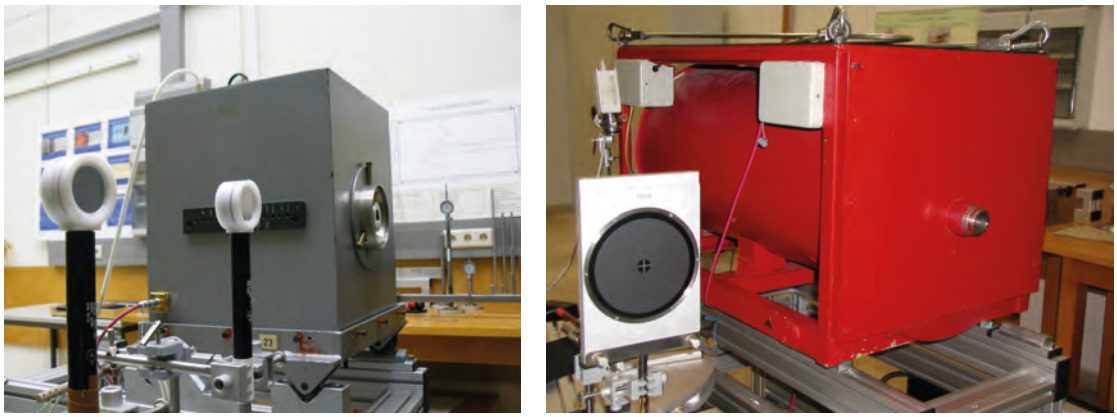

Figure 4: Calibration of secondary standards of typical ionization chambers for mammography with the PK100 (on the left) and for conventional radiography with the FK (on the right).

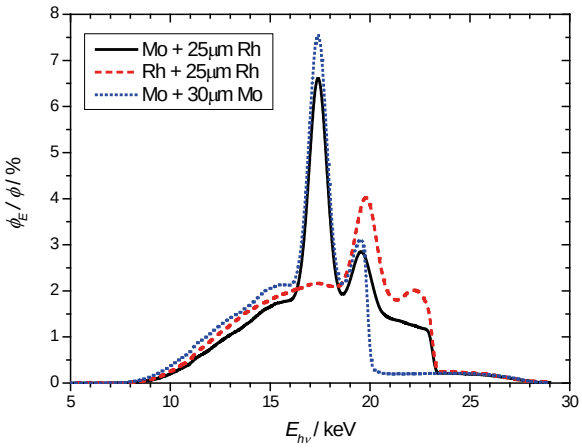

Figure 5: Typical photon fluence spectra of mammography radiation qualities at a tube voltage of 28 kV and with different combinations of anode and filter materials. The spectra were recorded with a high-purity germanium detector.

suring chambers are transparent, flat, parallel-plate ionization chambers which are an integral part of X-ray diagnostics equipment. The unit of the DAP is "Gy m²".

The dose yield of the X-ray tube assembly, related to the product of tube-current and time (in the unit "mAs"), is measured by means of dosimeters for radiodiagnostics in the useful beam of the X-ray device, free in air and in the unit "Gy/mAs". The incident dose is the dose at the surface of the beam entry side of the patient, without considering the scatter radiation caused by the body of the patient. The surface dose, in contrast, corresponds to the incident dose plus the dose caused by the scattered radiation. After having passed through the body of the patient, the X-rays reach the imaging system, where the image receiver dose is measured. The tissue-absorbed dose and the organ-absorbed dose are determined from the dose quantities via calculated conversion factors (see section 6).

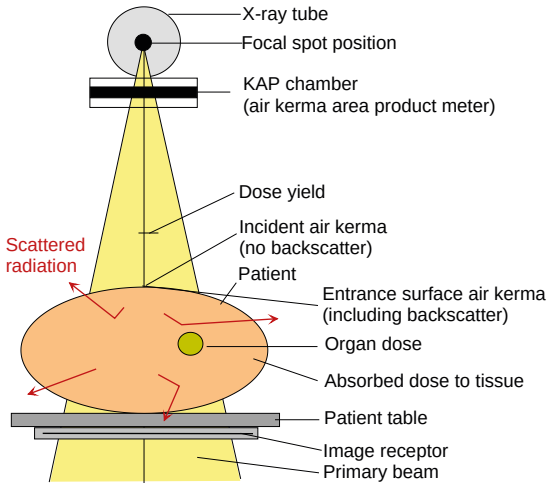

Figure 6: Schematic representation of classical projection radiography and the places where application-specific dose quantities are defined.

4.2 Mammography

The mammography is carried out with soft X-rays at tube voltages of approx. 25 kV to 35 kV. X-ray tubes with rotating anodes made of tungsten, molybdenum and rhodium are used, whereby the X-rays generated are filtered with foils of thin aluminium, molybdenum, rhodium, palladium or silver (depending on the system). The beam path on a mammography device (Figure 7) differs from classical projection radiography because, here, not the complete beam cone is used for the X-ray photograph, but only that half which is blocked on the side of the cathode. In this way, the radiation runs parallel to the chest wall. Due to the so-called "heel effect", the dose rate of the radiation decreases in addition – in accordance with the anatomy of the female breast – with the thickness of the mamma. The heel effect describes the decrease in the dose rate in the beam cone on the side of the anode.

In contrast to classical projection radiography, mammography does not include a DAP measuring chamber in the beam path because this would cause undesired, additional filtering of the soft X-rays. Therefore, the most important quantity is the incident dose, from which the organ-absorbed dose (soft-tissue-absorbed dose) is then calculated by means of conversion factors. The incident dose can be determined from the surface dose measured on a phantom by division with the backscatter factor. In quality assurance, also the image receiver dose plays a role.

4. 3 Computed tomography

The fact that – compared to classical projection radiography – the dose in computed tomography (CT) is clearly higher can be explained as follows: a CT image corresponds to approx. 1000 projections which are recorded during the rotation of the X-ray tube assembly around the patient.

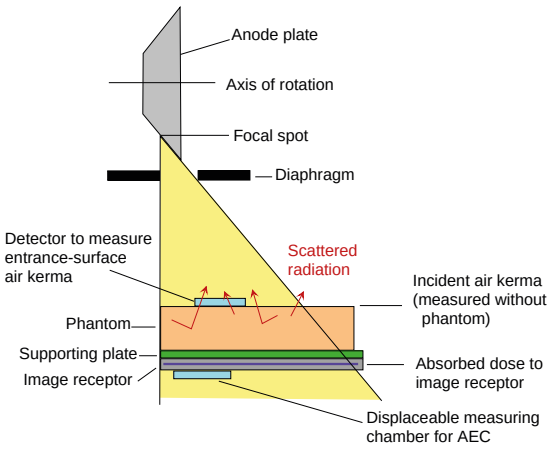

Figure 7: Schematic representation of the beam geometry on a mammography device and the places where the application-specific dose quantities are defined.

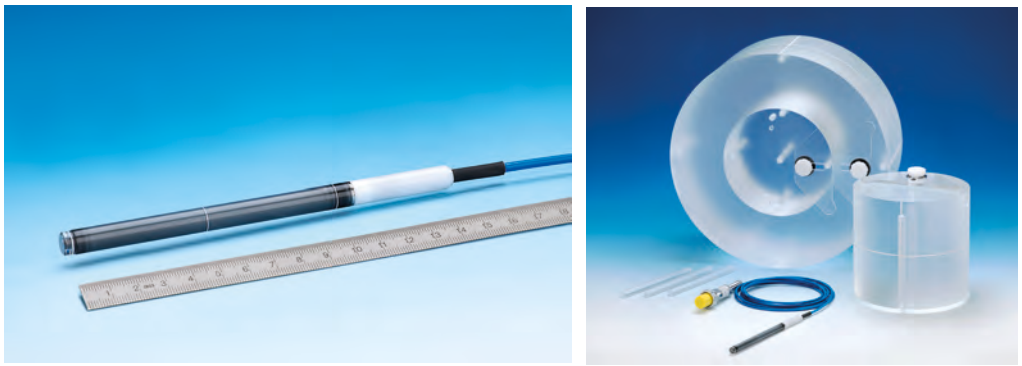

Figure 8: CT measuring chamber (left) and CT standard phantoms (right). The phantoms are made of plexiglass; they are 14 cm in length and have the following diameters: 16 cm (head phantom) and 32 cm (body phantom).

Dosimetry in CT is somewhat more complex than in classical radiography. Here, the so-called "CT dose index" (CTDI) is used as the quantity. The CTDI is the line integral of the air kerma along the axis of rotation (z-axis) of the scanner for a single radiator rotation, divided by the total collimation in z-direction. The CTDI is indicated in the unit "mGy". The measurement is performed with a pencil-shaped ionization chamber, 100 mm in length, which is also referred to as the "CT chamber" (Figure 8). The CT chamber is calibrated in the quantity "air kerma length product" in the unit "Gy · m". The CTDI is measured both free in air and also in cylindrical bodies on the central axis and at four peripheral positions (Figure 9). Cylindrical plexiglass bodies with diameters of 16 cm (head phantom) and 32 cm (body phantom) are in use (Figure 8). The head phantom is used for skull images and in pediatrics, whereas the body phantom is used for examinations on adults in the area of the trunk. A suitably weighted mean value of the CTDI values measured at the periphery and on the central axis is representative of the mean phantom dose in a layer and is referred to as the "weighted CTDI" (abbreviated to: "$CTDI_w$"). Usually, several layers are recorded either in series or spirally, whereby the patient table is moved while the tube is rotating. The ratio between the table's advance during a single radiator rotation and the total collimation in z-direction is referred to as the "pitch". Pitch values smaller than 1 thus indicate overlapping layers in CT images. Overlapping layers are associated with an increased dose per layer, which is taken into account by the pitch-corrected $CTDI_w$. This value is also called the "volume CTDI" (abbreviated to: "$CTDI_{vol}$"), or the "effective, weighted CTDI". A measure of the total dose of a scan series is the product of $CTDI_{vol}$ and the scan length L, which is also called the "dose length product" (DLP) of a scan series. For new CT devices, DIN EN 60601-2-44 prescribes the display of the $CTDI_{vol}$ and of the DLP. Common units are "mGy" for the $CTDI_{vol}$ and "mGy · cm" for the DLP.

The calculation of the patient dose is complex because it also depends on the body region that has been scanned. Similar to conventional radiography it is, however, derived from the measured CTDI values with the aid of calculated conversion factors.

As the technology in the field of CT is advancing very rapidly, CT dosimetry must keep pace. Due to an ever increasing scanning width in z-direction (keyword: "cone beam CT"), the conventional CT measuring chambers can no longer be used. Therefore, new approaches and approximations have been made in CT dosimetry which, for lack of space, are not represented in this article. In future, PTB will have a reference measuring set-up for CT dosimetry of its own at its disposal, to be able to check not only newer concepts, but – in particular – also novel detectors. These findings provide the basis for the establishment of requirements for novel CT detectors and measuring procedures, among other things for the type testing of CT dosimeters (see section 5).

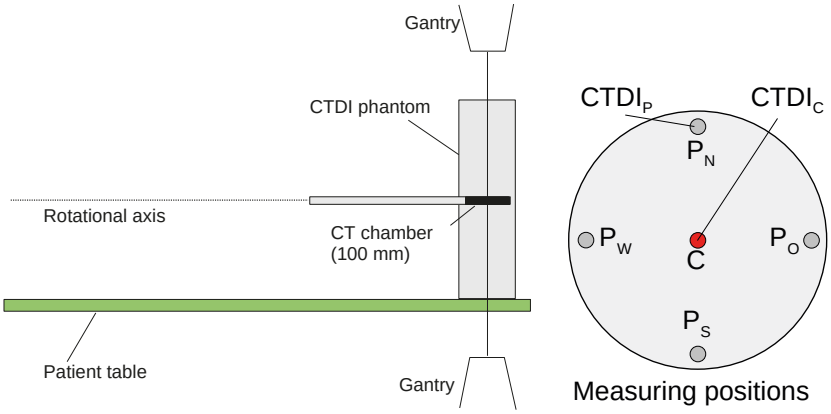

Figure 9: Schematic representation of the measurement of the CTDI by means of a CT chamber on the central axis of a cylindrical phantom body (left), as well as defined measurement locations on the periphery (P) and on the central axis (C) of the phantom.

5 Quality assurance in X-ray diagnostics

In Germany and at the international level, quality assurance for equipment in X-ray diagnostics is guaranteed by acceptance inspections and constancy tests. For this purpose, a great number of national and international standards exist for the different X-ray diagnostic modalities. During the acceptance test, checks are made as to whether a newly installed or a considerably modified device agrees, during its start-up, with the defined specifications. The constancy test comprises a number of tests to ensure the functional capability of the device in accordance with defined criteria. Thereby, a number of checks of the acceptance test are repeated and then compared with the results of the acceptance test to ensure an early detection of changes in the characteristics of the device. Of essential importance is the test which is aimed at checking whether the required image quality can be achieved with a predefined minimum dose. In this connection, measurements of the dose may be performed only with dosimeters for radiodiagnostics which comply with the requirements of the international standard IEC 61674. In Germany, Austria and Switzerland, dosimeters for radiodiagnostics which are used for acceptance tests are subject to legal control and require, therefore, an acceptance for verification. In Germany, this is the task of PTB. In the course of the pattern approval test, it is determined whether the dosimeter complies with the PTB requirements, which essentially agree with international standards. Through intensive cooperation in national and international standardization, PTB also participates in the elaboration of the relevant standards.

A second pillar of quality assurance is represented by the so-called "diagnostic reference levels" (DRLs). In the *Röntgenverordnung* (X-ray Ordinance – RöV), they are defined as "dose values for typical examinations with X-rays, related to standard phantoms or to groups of patients with standard dimensions, with X-ray equipment and examination procedures which are suitable for the respective type of examination". DRLs are determined and published by the *Bundesamt für Strahlenschutz* (Federal Office for Radiation Protection – BfS). The DRLs serve as upper standard values which must, on average, not be exceeded in the examination of humans. The medical authorities are obliged to notify any constant, unjustified exceeding of the DRLs to the competent state authority. DRLs for classical radiographs on adults and children have been published by the BfS in the quantity "dose area product" (see 4.1) in the unit "cGy*cm^2". DRLs for mammography have, however, been published as a mean glandular dose (see 4.2) in the unit "mSv". For CT examinations, the DRLs are indicated in the quantities "$CTDI_{vol}$" (see 4.3) in the unit "mGy", and the DLPs (see 4.3) are indicated in the unit "mGy · cm". To ensure the reliability of DRLs, it is indispensable for the dosimeters used to be calibrated traceably to primary standards.

6 Determination of the organ-absorbed dose and of the effective patient dose

The absorbed dose (unit: J/kg = Gy) in tissue or organs is the relevant quantity for the estimation of biological radiation damage. A distinction must be made between deterministic radiation damage and stochastic radiation damage. In X-ray diagnostics, the threshold dose of 0.2 Gy – 0.5 Gy, which may lead to deterministic radiation damage, is usually not reached, except in interventional examinations. The probability of stochastic radiation damage such as, for example, cancer or genetic damage, depends not only on the absorbed dose, but also on the radiation type (e.g. photons, electrons, neutrons, protons or alpha particles) and their energy. To take this fact into account, the absorbed dose is multiplied by so-called "radiation weighting factors", and the equivalent dose is obtained, whose unit (J/kg) is given the special name of "sievert" (Sv) to distinguish it from the physical absorbed dose. As the radiation weighting factor for photons is 1, the equivalent dose in X-ray diagnostics corresponds to the absorbed dose. In addition to the equivalent dose, the probability of stochastic radiation damage also depends on the type of tissue or organ, which is taken into account by the so-called "tissue weighting factors". The effective dose in partial or full-body irradiations is, therefore, obtained as the weighted sum of the equivalent dose to a tissue or organ. Values of the weighting factors for tissue and organs can be found in the literature [5]. As in X-ray diagnostics, the organ-absorbed dose or the tissue-absorbed dose of a patient cannot be measured directly, they are calculated from application-specific dose quantities with the aid of conversion factors. Conversion factors are, in this context, the organ-absorbed dose or the tissue-absorbed dose of a standard patient, normalized (in classical radiography) to the incident dose or the DAP or (in CT) to the CTDI. In mammography, the conversion factor is obtained as the mean glandular dose normalized to the incident dose. Such conversion factors are calculated almost exclusively with Monte Carlo simulations, in connection with defined models of standard patients [2]. As the determination of the effective patient dose is ultimately based on measurable dose quantities, correct calibration and quality assurance of the dosimeters for radiodiagnostics is of great importance in order to obtain reliable and comparable data.

7 Requirements for the uncertainties of dose measurements in X-ray diagnostics

In its Report 74 [2] entitled *Patient Dosimetry for X Rays used in Medical Imaging*, the ICRU (International Commission on Radiation Units and Measurements) writes:

"The uncertainty of dose measurements for comparative risk assessment as well as for quality assurance should not exceed about 7 % using a coverage factor of 2".

The requirements for the expanded uncertainties ($k = 2$) U in the metrological dissemination chain of the unit of air kerma, which result from this specification, are summarized in Figure 10. In the following, "uncertainty" always relates to the "expanded uncertainty". The typical uncertainty in the realization of the unit of air kerma by means of free-air ionization chambers for diagnostic X-rays (25 kV – 150 kV) lies at 0.6 % [3]. The calibration factor of secondary standards for the air kerma can be indicated with a typical uncertainty of 1 %. The air kerma measured in secondary standard laboratories is affected by typical uncertainties of approx. 1.5 %, and the calibration factors of the user dosimeters calibrated there with uncertainties of approx. 3 %. When the user dosimeters are used in clinical fields for the measurement of application-specific dose quantities, the uncertainties should lie in the range from 4 % to 7 % to comply with the ICRU specification.

Unfortunately, the actual uncertainties are often significantly higher when application-specific dose quantities are measured in clinical practice. This is, on the one hand, due to the deviations permitted in the requirement standards for the indicated value of the quantity as a function of different influence quantities such as the radiation quality, the direction of the beam incidence, the dose rate, the climatic conditions or the electromagnetic fields. If these permitted deviation limits are regarded as uncertainties with a rectangular distribution, the combined standard uncertainty of a dosimeter for radiodiagnostics already amounts, according to IEC 61674, to 6.5 %. This corresponds to an expanded uncertainty of 13 %! For DAP measuring chambers, the respective standard measurement uncertainty according to IEC 60580 even amounts to 12.5 %, i.e. expanded with $k = 2$ to 25 %! On the other hand, the problem can also be attributed to the conditions prevailing in clinical practice: if, during a measurement, many of the possible deviations caused by influence quantities are corrected with the aid of known correction factors, the uncertainties could be halved without any problems. Unfortunately, this, however, fails for lack of time and due to the increased costs. Possibly, the recommendation of the ICRU, which seems to be too strict for practical applications, should be discussed once again. There is, however, still great potential for further improvements of the user dosimeters. In any case, the achieved typical uncertainties of the primary and secondary standards seem to be sufficiently small in this connection. There are, in contrast, still significant optimization possibilities for the measurement or determination procedures of the application-specific dose quantities.

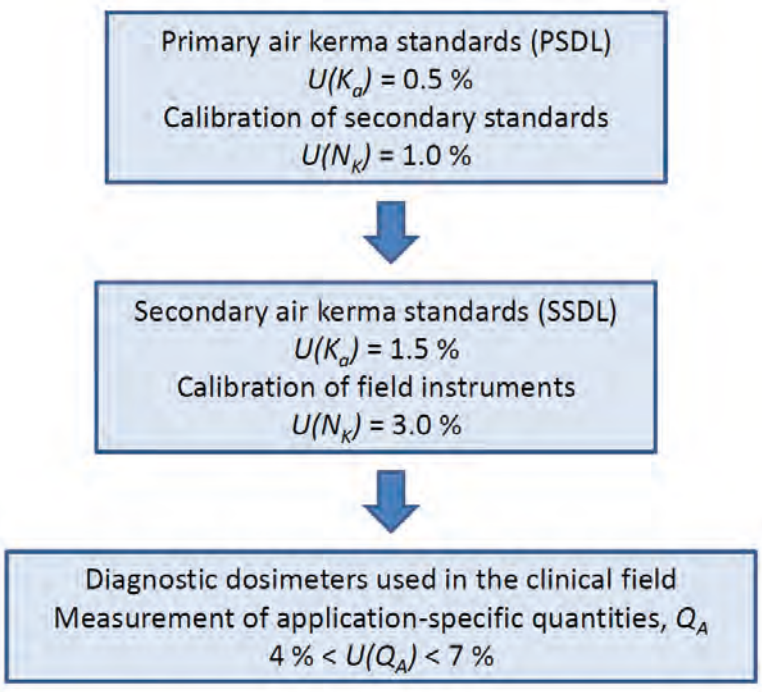

Figure 10: Expanded uncertainties ($k = 2$) in the metrological chain from the primary standard to application-specific dose quantities in X-ray diagnostics.

8 Summary

Almost half of the radiation the German population is exposed to and which is caused by ionizing radiation from natural and artificial sources originates from X-ray examinations. *Dosimetry in X-ray diagnostics* is, therefore, of particular importance. The purpose of dosimetry in X-ray diagnostics is, on the one hand, to ensure quality control according to the state of the art of science and technology and, on the other hand, patient dosimetry to estimate the risks arising from radiation exposure. The fundamental quantity of dosimetry is the air kerma, which is primarily measured with the aid of free-air ionization chambers. From the air kerma, the application-specific dose quantities are derived, for example, the incident dose and the dose area product for projection radiography, and the dose length product for computed tomography. These establish the basis for dose measurements within the scope of quality assurance by means of acceptance inspections and constancy tests and for the determination of diagnostic reference levels. The

latter serve as upper standard values which must, on average, not be exceeded in the examination of humans. However, also the organ-absorbed dose and the tissue-absorbed dose of standard patients are determined from the application-specific dose quantities with the aid of calculated conversion factors. The effective patient doses calculated from these are used for risk assessments in comparison with radiation exposures from other sources of ionizing radiation. According to a recommendation of the ICRU, dosimetry in X-ray diagnostics should, for the purposes mentioned, be carried out with an expanded uncertainty ($k = 2$) of not more than approx. 7 %. Even if the uncertainties of the primary and secondary standards already seem to be sufficiently small (approx. 0.6 % and 1.5 %), this specification has, by far, not yet been implemented in clinical practice, where uncertainties of up to 25 % are still found.

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Activity Determination of Radionuclides for Diagnosis and Therapy

Karsten Kossert*

Abstract

In medicine, the use of radionuclides plays an important role and requires reliable activity determinations. For this purpose, PTB makes activity standards available and determines the activity on submitted sources. This article describes how activity determinations are performed at PTB and in which ways they can be used for nuclear medicine. Research and development work at PTB is described, as well as the determination of some isotopes that are relevant to medicine.

Introduction

In medicine, a great number of radionuclides are used for diagnostic procedures such as scintigraphy or positron emission tomography (PET). With the aid of these imaging methods, tumours can be made visible; but the spectrum of applications also covers examinations of blood vessels, tissue or bones. The radionuclide most frequently used for diagnostic examinations is technetium-99m. Numerous relevant substances can be marked with technetium-99m and can then be used for different organ examinations. In therapy, too, radionuclides play an important role. In some measures, tumour tissue is purposefully destroyed by the ionizing radiation emitted by the radionuclides. A well-known example is the treatment of thyroid problems with radioactive iodine, which is absorbed in the body mainly by the thyroid tissue. A – still rather new – method is the so-called *radioimmunotherapy*. Hereby, radionuclides are coupled to suitable antibodies which specifically adhere to tumour cells. But also palliative applications, such as *radiosynoviorthesis* (RSO), are often carried out in order to improve, for example, the quality of life of rheumatism patients. As the radiopharmaceutical administered to the patient leads to a considerable radiation exposure, special care must be taken when deciding on the treatment. The risk-benefit analysis usually yields that the radionuclides that are suitable must have a biological and physical half-life that is as short as possible.

Reliable activity determinations are of great importance for the use of radionuclides because both the success of the application and the radiation exposure of a patient depend on them [1–3]. Activity standards are also legally prescribed for the calibration of radiation-protection measuring instruments which are used in nuclear-medical companies [4].

Activity standards of PTB

The determination of radionuclides used in nuclear medicine is one of PTB's most important tasks in the field of radioactivity. For this purpose, PTB annually provides activity standards for some of the – mostly short-lived – radionuclides. It is, however, also possible for nuclear-medical companies to submit sources, whose activity is then determined at PTB. Ultimately, both possibilities serve to ensure that the measuring systems used in nuclear medicine will be traceably calibrated.

The measurement procedures applied to determine the activity of radioactive sources are manifold. This is, in particular, due to the different decay properties of the relevant radionuclides. At PTB, liquid scintillation counting has developed into one of the most important methods. Thereby, mainly the so-called CIEMAT/NIST method as well as, for some years, the TDCR method (*triple-to-double coincidence ratio*) have been used [5]. One method for activity determination, which is important now as before, is the 4πβ-γ coincidence measurement. Hereby, liquid scintillation counters increasingly replace the proportional counter which was previously used for the detection of beta radiation.

The above-mentioned methods are referred to

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Figure 1: Activity standards of PTB are, among other things, manufactured and offered as aqueous solution in sealed-off glass ampoules.

as *absolute measurement procedures* or as *primary standard methods*, as the activity of a radionuclide can be determined without any other activity standard of the same nuclide. Some of the methods require, however, extensive work for source preparation and great care in the measurements. Apart from this, the evaluation of the measurement data is very complex and time-consuming.

To avoid having to apply the laborious *absolute measurement procedures* to every activity determination, *secondary measurement procedures* are used for most of the calibrations. These are also called *relative measurement procedures*. In addition to semiconductor spectrometers and sodium iodide detectors, mainly ionization chambers are used at PTB for relative measurements of the activity. A combination of an ionization chamber and a current measuring device, called "activimeter", is also often used in nuclear medicine. This designation has largely replaced the obsolete name "curiemeter".

The activity standards manufactured by PTB are offered in different geometries. In addition to solid sources (which are often offered as point sources), the aqueous solutions in sealed-off glass ampoules (which are shown in Figure 1) rank among the most frequently provided activity standards. The activity of the solutions is determined by absolute measurements or by measurement with calibrated 4π-ionization chambers of PTB.

In the past few years, PTB has participated in international comparison measurements for many radionuclides in order to render proof of its competence in the field of activity measurements and to guarantee international recognition of calibration certificates. The basis of this is the *Mutual Recognition Arrangement* (MRA), which has been concluded within the scope of the work of the *Comité International des Poids et Mesures* (CIPM). The CIPM-MRA [6] is a worldwide agreement on the mutual cross-border recognition of calibration certificates issued by national metrology institutes for commercial or socially relevant measurands. The agreement serves to remove barriers to trade and requires that – besides proving the use of a quality management system – the participants take part in comparison measurements. For the unit of activity, such comparison measurements are carried out by sending aliquots (equivalent samples) of a radioactive stock solution of a nuclide to the participants in the comparison. The participants then determine the specific activity as well as any possibly existing radioactive impurities and send the results, including a complete documentation and an uncertainty analysis, to the *Bureau International des Poids et Mesures* (BIPM) in Paris, where the data is then evaluated.

Furthermore, the international reference system SIR (*Système International de Référence*) for activity measurements was established in 1976 at the BIPM [7]. In the case of this system, the participants fill ampoules made available by the BIPM with their national activity standards in the form of solutions or gases and send them to the BIPM in Paris. There, the ampoules are measured in an ionization chamber and compared with a long-lived ^{226}Ra reference source. Due to the traceability of the measurement values to the ionization current of the radium reference source, and due to the excellent long-term stability of the measuring system associated with this, the results of the participants can be compared with one another, even if there are periods of several

years between the submissions of the individual institutes. Until 2013, approx. 950 samples of more than 60 different radionuclides had been submitted and measured. PTB made a particularly great contribution to this, because 60 ampoules with solutions of 38 radionuclides came from Germany. The SIR system offers a great number of advantages: Firstly, the national institutes which are responsible for metrology gain more flexibility in timing their comparison measurements. The selection of the radionuclides as well as the number of the comparisons can be adapted to their own efficiency. But above all, it allows comparisons to be performed on rather short-lived radionuclides. PTB, for example, succeeded in sending ampoules of the isotopes technetium-99m and fluorine-18 with half-lives of approx. 6 hours or even only 110 minutes to the BIPM [8, 9]. For a worldwide distribution of corresponding solutions, the logistic problems are, however, often insuperable due to the transport times.

The proven calibration and measurement capabilities of PTB have recently been summarized in a so-called "CMC Table" (*Calibration and Measurement Capabilities*). After an assessment process of several stages, this Table was accepted and published at the BIPM [10]. In most cases, entries in the CMC Table require participation in comparison measurements for the respective radionuclide. For radionuclides with similar decay properties and similar absolute measurement procedures, an entry may, however, also be justified by tables of the *radionuclide measurement methods matrix* [11]. These tables classify radionuclides in accordance with the measurement procedure and the severity level, and they allow the national metrology institutes to furnish proof of the calibration and measurement capabilities also indirectly by comparison measurements of other radionuclides, if these have an identically high or a higher severity level of the measurement procedures and can be measured with similar methods.

Due to the enormous number of comparison measurements and due to the always good results obtained therein, PTB is among the worldwide leading metrology institutes in the field of radionuclide metrology. In this connection, it must be taken into account that in many comparison measurements, radionuclides are measured which are relevant to nuclear medicine. Examples of this are the following isotopes which are relevant to medicine: fluorine-18, copper-64, yttrium-90, technetium-99m, indium-111, iodine-131, lutetium-177, rhenium-186 and thallium-201 which have been successfully measured at PTB in the past 10 years within the scope of comparison measurements.

Determination of radionuclide data

At PTB, the activity measurements are often combined with other measurement procedures in order to determine radionuclide data experimentally. Frequently, also the half-lives of radionuclides are determined by long-term measurements [12-14]. Such radionuclide data are important for other measurement procedures and for the estimation of the radiation exposure. An exact knowledge of the decay properties is very important especially in experiments which are aimed at establishing "new" radionuclides for medical procedures. In the following, it will be shown by means of the example of lutetium-177 how radionuclide data are determined at PTB.

The beta-ray emitter lutetium-177 is used for tumour treatment in nuclear medicine. Due to the emissions of photons from the gamma transitions, it can also be used for imaging procedures, so that the therapeutic benefit is supplemented.

Recently, PTB has been one of eleven participants in an international comparison and has used three measurement procedures for activity determination. The combination of the three measurement procedures allowed PTB to achieve the smallest relative standard measurement uncertainty of the comparison (0.19 %). In addition, the result excellently agrees with the mean value of all participants in the comparison. The combination of the exact activity measurements and of measurements of the photon emissions by means of well-calibrated semiconductor spectrometers allowed photon emission probabilities to be determined [15]. The half-life of ^{177}Lu was redetermined by a long-term measurement with a liquid scintillation counter. The result is in good agreement with former measurements and improves the database. The value now recommended for the half-life amounts to $T_{1/2}$ = (6.6457 ± 0.0030) days [15].

The reproducibility of the activity measurements at PTB is confirmed by relative measurements with 4π ionization chambers which – quasi – allow the conservation of the former absolute measurements. At PTB, the ionization chamber measurements of a radionuclide are – similar to the SIR at the BIPM – always carried out together with measurements of a long-lived ^{226}Ra standard, so that possible variations in the response are largely compensated for. As the response depends, among other things, on the measurement geometry used, the latest absolute measurements have also been used to determine calibration factors of a new ampoule type which has only been used at PTB since 2005. In this way, PTB will, also in future, be able to carry out activity determinations by means of calibrated ionization chambers and to guarantee the dissemination of the unit of activity for ^{177}Lu. An important prerequisite for quality-ensured

applications in nuclear medicine has thus been met.

Similar to lutetium-177, nuclear data of other isotopes have been determined at PTB in the past ten years. Many of them are of great importance especially for medicine. Among them are copper-64 [14] and yttrium-90 [13].

New ways from PTB to the patient

The possibilities frequently used for the calibration of measuring instruments in nuclear medicine have already been mentioned: The provision of activity standards as well as the calibration of submitted sources. For some years, a third possibility has been increasingly utilized: The ionization chambers often used in medicine can be calibrated directly at PTB. This possibility is in high demand on the part of the manufacturers of the ionization chambers. In a large-scale project which has only recently been completed, three ionization chambers of a manufacturer were investigated by PTB in detail [16]. The investigations covered the long-term stability, the linearity of the respective electrometers for the measurement of the ionization current, and the geometry dependencies. In addition, the experimentally determined calibration factors of a great number of radionuclides were used to determine functions for the energy-dependent response of the ionization chambers. With the energies and emission probabilities of the respective photons and electrons which may be emitted as a result of the radioactive decay, these functions can be used to calculate calibration factors for other radionuclides. This is useful, in particular, if an experimental determination of calibration factors of a radionuclide is not possible. Examples are: thallium-200 and thallium-202. These occur as impurities in solutions of the isotope thallium-201, which is important for nuclear medicine, and require corresponding corrections of the measurement data [16].

PTB has, however, also calibrated ionization chambers which are used as secondary standard measuring devices at other national metrology institutes. In the past 10 years, this was the case for the countries Bulgaria [17], Slovakia and Turkey. The calibrations are often carried out for several radionuclides. For quality assurance, a large number of repeat measurements are required. In addition to the radioactive sources of the respective isotopes, reference sources of long-lived radionuclides and sources without radioactivity are also measured to take the so-called background into account. At PTB, the great number of measurements can be coped with by measuring systems with automatic sample changers (Figure 2). For the measurements, the systems are fitted with several sources and then measured with a fully automatic system. The measurements can be performed around the clock, and the radiation exposure for the staff is reduced to a minimum. To better satisfy

Figure 2: PTB's measuring set-up with two ionization chambers and an automatic sample changer.

the increasing requirements for such calibrations, an improved system is presently being established which will allow up to four ionization chambers to be calibrated simultaneously.

National technetium-99m comparison

To meet the requirements of the Mutual Recognition Arrangement, PTB constantly furnishes proof of its measurement capabilities by participating in international comparison measurements. But how do these capabilities compare in practical nuclear-medical applications in Germany? To obtain information about this, a national comparison was, for the last time, carried out in 2006 on the basis of technetium-99m [8]. Within the scope of that comparison, ampoules with a solution of this isotope were sent to the participants who had to determine the activity. The results of the participants were then sent to PTB, where they were evaluated. This evaluation showed that 92 % of the participants achieved results which deviated by less than 10 % from the reference value of PTB. These participants thus meet the requirements of the European Pharmacopoeia [18]. All participants reached deviations from the PTB value of less than 20 %. At the same time, PTB sent an ampoule to the SIR system at the BIPM in Paris to confirm the accuracy of its own measurements. The result determined at PTB with a relative standard uncertainty of only 0.41 % deviates by less than 0.3 % from the international reference value (*key comparison reference value*).

In addition, the data of the national comparison were checked in order to detect any possible causes of discrepancies. In that context, it could be seen that large deviations were – in many cases – not attributable to the measuring equipment, but to insufficiently qualified staff. Some of the deviations can, for example, be explained by the fact that the activity values determined had not (or only insufficiently) been corrected with respect to the radioactive decay. The reports also showed that 38 % of the participants did not make any statement on the measurement uncertainty. Several participants indicated uncertainties which were too small, others reported a relative uncertainty above 10 % and, thus, did not meet the requirements of the European Pharmacopoeia [18]. The quality of measurements in medicine can surely be improved by more frequent comparison measurements of this kind. In Germany, participation in such intercomparisons is, however, voluntary.

Research and development for medicine

Reliable activity measurements are based on the absolute measurement procedures mentioned above. At PTB, the corresponding measurement procedures are constantly being improved and expanded in order to reduce the uncertainties further and to make suitable methods for "new" radionuclides available. In the past few years, especially liquid scintillation counting has been developed with great success. The success is largely based on newly developed TDCR devices which are equipped with a coincidence electronics system developed at PTB. Meanwhile, a TDCR system of PTB has been equipped with an automatic sample changer so that here, too, many measurements can be carried out with little effort and a low exposure rate. As a counterpart to this apparatus, which has the size of a wardrobe, a mini TDCR apparatus has also been established at PTB. The core piece is accommodated in a suitcase, and the complete electronics can be comfortably transported in a passenger car. This will, in future, also make it possible to carry out measurements at the production sites of very short-lived radionuclides which, due to their half-life of a few minutes, cannot be transported to PTB. Among these radionuclides are the PET nuclides carbon-11, nitrogen-13 and oxygen-15.

Like the CIEMAT/NIST method, the TDCR method was originally developed for pure beta-ray emitters. However, in the past few years, the models have been constantly expanded to allow also detection probabilities of electron capture nuclides or simple beta-gamma nuclides to be calculated. As a result of the latest development work of PTB, a computer program is now available by means of which detection probabilities of radionuclides with very complex decays can be calculated. Thereby, TDCR measurements can now also be performed for isotopes such as iron-59, iodine-131, lutetium-177, rhenium-186 or rhenium-188.

In a new procedure developed at PTB, the activity of high-energy beta-ray emitters is even measured without scintillation liquid. The TDCR Čerenkov method [19] exploits the fact that high-energy electrons from beta decay generate Čerenkov light in a dielectric, transparent medium such as, for example, water if their velocity is higher than the phase velocity of the light. From the field of medicine, the radionuclides phosphor-32, strontium-89, yttrium-90 and ruthenium-106/rhodium-106 rank among the high-energy beta-ray emitters which can be measured with the method without the necessity of mixing the solutions to be investigated with an organic scintillator. This reduces the material costs, and mixed radioactive waste – whose disposal is very complex and expensive – is prevented. The

high-energy beta-ray emitter yttrium-90 is, among other things, used with so-called *microspheres* for the treatment of liver cancer. The TDCR Čerenkov method is to be also applied to the activity determination of the respective radiopharmaceuticals.

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Dosimetry for Brachytherapy

Ulrike Ankerhold*, Thorsten Schneider**

Brachytherapy (Greek: brachys = close) is a method of radiation therapy where one or several small radiation sources – almost exclusively radionuclide sources – are placed either very close to, or in contact with, or directly into the tumour. Brachytherapy dates back to the year 1901. Already shortly after the detection of radioactivity by Becquerel in 1896, radioactive sources were inserted into a tumour, and it was observed that radiation made the tumour shrink [1]. In the early 20th century, new application techniques were developed by Danlos at the *Institut Curie* in Paris and by Robert Abbe at the Memorial Hospital in New York [2][3] which used radium. After the initial interest in brachytherapy in Europe and in the USA, its use declined in the middle of the 20th century. The reason for this was the radiation exposure of the medical personnel due to the manual handling of the sources.

The development of remote-controlled afterloading systems and of new brachytherapy sources in the 1950s and 1960s clearly improved source handling and radiation protection. This, as well as new developments in the field of three-dimensional imaging methods, automated treatment planning, and the enhancement of the afterloading systems have turned brachytherapy into a safe and efficient form of treatment for many cancer types [1]. It is often used to treat cervical cancer, prostate cancer, breast cancer and skin cancer.

Brachytherapy can be used alone or in combination with other forms of therapy, e.g. surgery, external radiation therapy and chemotherapy. Studies prove that the cure rates of cancer which are due to brachytherapy only are comparable to those due to a surgery or external radiation therapy [4]. The risk of side effects is, however, clearly lower in brachytherapy [7].

When using this treatment method, the radiation source can be very diverse: radioactive beta, gamma and X-ray emitters[1] and, recently, also miniaturized X-ray tubes. Since the first treatment with brachytherapy, the radionuclides given in Table 1 have established themselves for clinical use.

In general, radioactive brachytherapy sources are constructed as small cylindrical sources with a length of up to 0.5 cm. The radioactive material is usually enclosed by a titanium shell. The interior structure of the sources is manufacturer- and type-specific. The sources are classified into the two categories “high dose rate (HDR) sources” and “low dose rate (LDR) sources”.

Sources which provide a dose rate of more than 12 Gy/h at a depth of 1 cm in water are designated as “high dose rate sources” (HDR sources). In this field, the radionuclide ^{192}Ir has established itself as a source material. Lately, ^{60}Co has experienced a renaissance. Due to its longer half-life time, its use offers economic advantages. For ^{60}Co sources, however, much higher radiation protection precautions must be made than when using ^{192}Ir sources. Sources which provide less than 2 Gy/h at a depth of 1 cm in water are designated as “low dose rate sources” (LDR sources), so-called LDR seeds. They are implanted in the tumour permanently or temporally. ^{125}I and ^{103}Pd seeds are mainly used.

A considerable advantage of brachytherapy is that due to the fact that the sources are being placed in the tumour or next to it, a high dose can be deposited in the tumour and, at the same time, healthy tissue which is located further away from the tumour can be spared. In the case of radiation penetrating from outside (external radiation therapy), also healthy tissue is inevitably exposed.

The objective of radiation therapy is to generate in the tumour a sufficiently high – and as homogeneous as possible – dose distribution. In brachytherapy, this is achieved by using several sources simultaneously and/or by modifying the position of the source during a patient’s irradiation period.

1 X-ray emitter: Radionuclides emitting photon radiation with energies of up to approximately 300 keV.

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Radionuclide	Radiation	Half-life time	Maximum energy	Mean energy
Caesium-137	Photon radiation	30.17 years	661 keV	614 keV
Cobalt-60	Photon radiation	5.26 years	1.33 MeV	1.253 MeV
Iridium-192	Photon radiation	74.0 days	612 keV	371 keV
Iodine-125	Photon radiation	59.6 days	35.5 keV	28 keV
Palladium-103	Photon radiation	17.0 days	23.2 keV	21 keV
Ruthenium-106	Beta radiation	1.02 years	3.54 MeV	

Table 1: Properties of the radionuclides mainly used in clinical brachytherapy [5][6].

Realization and dissemination of the dose rate in brachytherapy

The dosimetric measurand in brachytherapy is the absorbed dose rate to water D_w at a distance of 1 cm from the centre of activity of the source, vertically to the source axis. Its value is derived from the value of the reference air kerma rate (RAKR), multiplied by the dose rate conversion coefficient Λ, also called "dose rate constant" [8][9]. The reference air kerma rate is defined as the air kerma rate free in air, at a distance of 100 cm from the source's centre of activity (vertically to the source axis) [9].

The value of the dose rate conversion coefficient is type-specific, i.e. it is identical for all sources of the same type. Until recently, the value could only be determined mathematically, by means of radiation transport calculations on the basis of Monte Carlo simulations. These values can be found in freely accessible data bases for all source types which are frequently used. Within the scope of more recent research projects, it has been possible for the first time to determine these values also experimentally for several HDR and LDR sources. The results achieved so far show a good agreement between the calculation and the measurement.

To achieve as successful a therapy as possible and to keep, at the same time, the risk for the patient low, traceable and quality-assured dosimetry is of great importance. The basis for this is the primary realization of the unit of the dose rate measurand and its dissemination by calibration of secondary standards or of brachytherapy sources. HDR and LDR sources are currently calibrated routinely at PTB in the unit of the reference air kerma rate (RAKR).

For more than 15 years, ^{192}Ir HDR brachytherapy sources have been calibrated at PTB in the measurand RAKR, with a relative standard measurement uncertainty of 1.25 % ($k = 1$).

In the case of the calibration of **HDR sources**, the air kerma rate is measured by means of an ionization chamber which is traceable to the primary standards of PTB for the air kerma free-in-air (see the article "Metrological Aspects of Dosimetry in X-ray Diagnostics" in this publication). The measurements are carried out in the collimated radiation field of the source. For this purpose, a special measurement unit was set up (see Figure 2). In the centre of a lead box (dimension: 30 cm × 30 cm × 40 cm; wall thickness: 5 cm), which is equipped with a DensiMed® diaphgram with an aperture of optionally 5.5 cm or 11 cm, the source to be calibrated is put in place using an afterloading system. The positioning of the calibrated sphere ionization chamber on the central axis of the radiation field defined by the diaphragm is carried out by means of a commercial industrial robot, with an uncertainty of less than 0.1 mm. To eliminate uncertainties which occur due to the positioning of the source by the afterloading system (approximately 0.3 mm), several measurements are performed at various distances between the radiation source and the ionization chamber, and the positioning of the source is determined by a calculation.

Within the scope of a European research project, a primary standard was set up for the realization of the absorbed dose rate to water for HDR brachytherapy sources. By means of water calorimetry (see the article "Calorimetric Determination of the Absorbed Dose to Water" in this publication), the absorbed dose rate to water can be determined in the near field of the sources [10]. The detector used in the calorimeter (Fig. 2) is based on the detector used in water calorimetry for high-energy fields. In order to achieve an exact and reproducible positioning of the source in front of the detector, the source is inserted into a stainless steel needle (inner diameter: 1.35 mm) which can be fixed very precisely in front of the detector at various

Fig. 1: Measurement set-up for the calibration of HDR brachytherapy sources in collimated radiation geometry. Afterloading system (left), lead box (rear centre), ionization chamber (black, centre), industrial robot (right).

distances (minimum distance: 24.35 mm) [10]. From the measurements taken at various distances, the absorbed dose rate to water is determined at a distance of 1 cm from the source.

In the case of the calorimetric measurements, the following effect interferes: radioactive HDR sources heat up due to the self-absorption of gamma radiation and/or due to the energy dissipation of the electrons in the source material. The taking into account of this "self-heat" is one of the greatest challenges (besides the steep depth dose distribution in the detector) of the absorbed dose rate to water realization by means of calorimetry.

The direct realization of the absorbed dose rate to water for HDR sources was used to experimentally determine the value of the dose rate constant Λ and, thus, to verify the calculated values. The values experimentally determined for selected types of ^{192}Ir sources show good agreement with the calculated ones [11].

The realization by means of water calorimetry is experimental and – if a low uncertainty is to be attained – also very time-consuming, which explains why this procedure is not suited for a direct routine calibration of individual sources.

Due to the stability of the value of the dose rate constant, which only depends on the type of the source, the absorbed dose rate to water should, also in future, be disseminated in brachytherapy via the calibration of HDR sources in the unit of RAKR, by using experimentally validated values of the dose rate constant.

Fig. 2: Detector element for the water calorimeter to realize the absorbed dose rate to water for HDR brachytherapy sources.

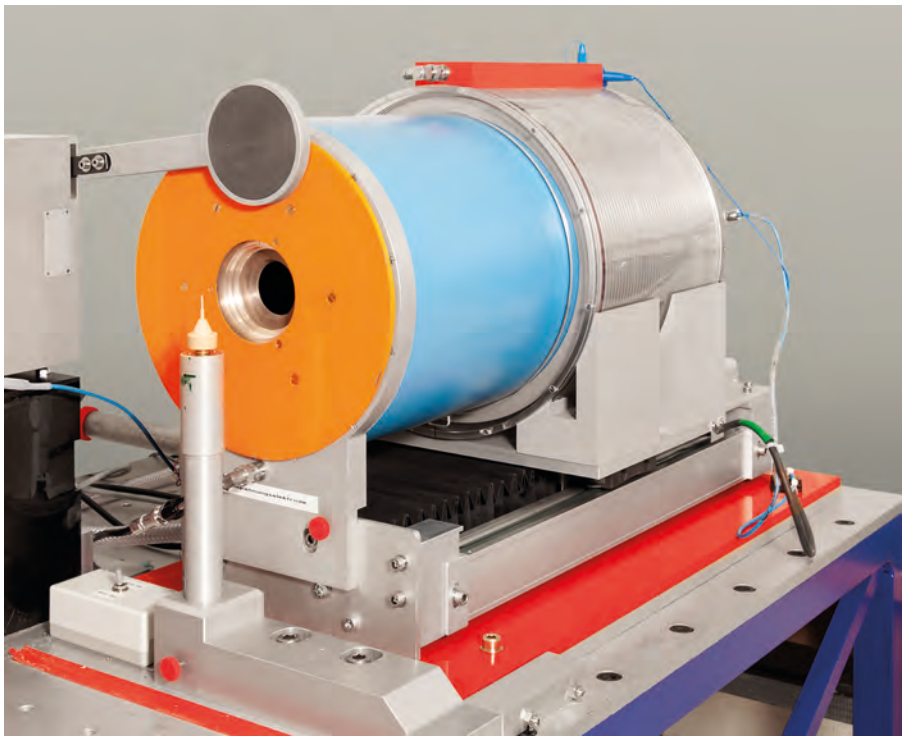

Fig. 3: View of the extrapolation chamber (so-called GROVEX I) for the realization of the reference air kerma rate (RAKR) for LDR sources in brachytherapy

Due to the low-energy photon radiation and the low dose rate, the dose rate measurand for **LDR sources** must be realized and disseminated in another way than for HDR sources.

For the realization of the reference air kerma rate (RAKR) of LDR sources, PTB operates an ionization chamber as a primary standard in the form of a large-volume parallel-plate extrapolation chamber (so-called GROVEX I) (see Figure 3). The front electrode (high-voltage electrode) and the rear measurement electrode are 12-µm-thin graphitated polyethylene foils [12]. The source is located at a distance of 30 cm from the front high-voltage electrode. In front of the high-voltage electrode, a lead diaphragm is installed to limit the radiation field of the source which enters into the chamber measurement volume. The distance between the electrodes can be freely varied to be able to measure the ionization current at various distances. The RAKR is determined from the slope of the straight line which is adapted to the measurement points.

The realization of the unit of the absorbed dose rate to water for brachytherapy using LDR sources – and also for using HDR sources – was realized within the scope of a European research project and established at PTB [13]. It is realized by means of ionometry using a large-volume coplanar plate extrapolation chamber. Its set-up and operation resemble that of the primary standard for the reference air kerma rate; however, the extrapolation chamber is located in a phantom

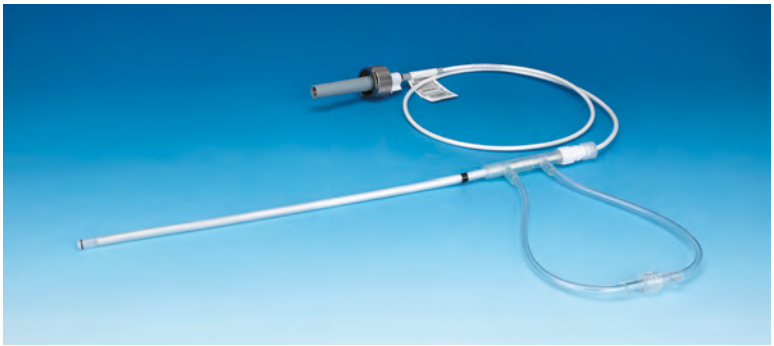

Fig. 4: Two different types of miniature X-ray tubes. Right: Intrabeam X-ray facility (Zeiss), left: AXXENT X-ray facility (Xoft).

made of water-equivalent material. Thus, the measurement method differs from that of the RAKR primary standard. It was developed on the basis of the radiation transport theory and – following an old-established idea – aims at the differences of current values at various plate distances [14]. The evaluation procedure uses quantities whose values were determined by means of Monte Carlo simulation. As these values are based on the ratios of calculated air kerma values within the extrapolation chamber, this method is very stable against uncertainties of the atomic interaction cross sections and the spectra [14]. The developed method was adopted by the Italian national metrology institute ENEA which also took part in the research project [15].

With the direct realization of the unit of absorbed dose rate to water, a measurement uncertainty of 2.6 % ($k = 2$) was achieved which – compared with the uncertainty of 10 % ($k = 2$) for the determination of the absorbed dose rate to water via the reference air kerma rate – is a clear reduction in the uncertainty. In contrast to HDR brachytherapy, a direct calibration of sources in the unit of the absorbed dose rate to water is feasible and is aimed at for LDR brachytherapy.

A new development in brachytherapy is the use of miniature X-ray tubes with a maximum tube voltage of 50 kV (see Fig. 4) which are directly inserted into the patient's body. Various types are commercially available and are used in hospitals. At present, miniature X-ray facilities are most frequently used for the intraoperative irradiation of mastocarcinoma. After a surgical excision of the tumour tissue, these tubes are placed in the cavity which has emerged, and the surrounding tissue is irradiated for about 25 minutes to kill tumour cells which might still exist.

The realization of traceable dosimetry for therapy with these X-ray facilities is the object of a research project which is currently being implemented within the scope of the "European Metrology Research Programme" of the European national metrology institutes.

To realize the unit of the absorbed dose rate to water in the radiation field of the miniaturized X-ray tubes, the primary standard for the realization of the absorbed dose rate to water for LDR sources is further developed. To disseminate the dose rate to hospitals, measurement procedures are being elaborated. The aim is to elaborate a standard or a protocol for medical physicists for dosimetry when using miniature X-ray facilities.

Another current focus of research – also within the scope of the above-mentioned European research project – is dosimetry in clinical fields of brachytherapy using HDR sources. HDR sources are mostly used in hospitals in combination with so-called "applicators". Applicators are auxiliary means for positioning the source in the patient's body and for shaping the radiation field, for example to shield radiation-sensitive tissue near the tumour from the radiation field and to spare it in this way. The respective applicator type used depends on the tumour geometry and on its location in the body. In the present protocols for clinical dosimetry and in treatment planning systems, the influence of the applicators on the dose applied is not taken into account [8].

The determination of the spatial dose rate distribution in typical clinical radiation fields of HDR brachytherapy (i.e. HDR sources using applicators) with an adequately low measurement uncertainty is a great metrological challenge. For this purpose, a 3D measurement system is under construction with which dose measurements with an uncertainty of only a few percent shall be possible. The activities are performed in cooperation with national and international organizations of medical physicists.

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Calorimetric Determination of the Absorbed Dose to Water

Achim Krauss*

1 Introduction

The absorbed dose to water D_W is the basic measurand in dosimetry for radiation therapy. In clinical operation, this measurand is usually determined by means of dosemeters, e.g. by ionization chambers of different configurations or by semiconductor detectors which have been calibrated in terms of absorbed dose to water under reference conditions in a 10 cm × 10 cm extended ^{60}Co radiation field. The calibration factors of these detectors are, thereby, traceable to PTB's primary standard measuring device for the realization of the unit of absorbed dose to water. PTB's primary standard measuring device is based on the use of a water calorimeter. The calorimeter is able to determine the absorbed dose to water at ^{60}Co radiation under reference conditions with a combined standard measurement uncertainty of 0.2 % [1]. Compared to international primary standards for the absorbed dose to water which are, in part, based on different measurement procedures [2], PTB's water calorimeter ranks at the top of the list [3].

The calorimetric determination of D_W is basically carried out independent of the energy and of the type of radiation. This opens up a broad field of application to water calorimetry as a standard measuring procedure for the determination of D_W. Besides the use in the case of ^{60}Co radiation, further applications arise for a major part of the radiation qualities and radiation conditions used in external radiological therapy, e.g. for X-rays of medium energy [4], for heavy-ion radiation, or for high-energy photon and electron radiation. This is the case, e.g., for the experimental determination of the energy-dependent correction factors (e.g. k_Q, k_E) for the change of the response of the users' dosemeters (e.g. ionization chambers) in high-energy photon or electron fields [5]. This also applies to special investigations with regard to the response of dosemeters as a function of the field size. Another field of application is the dosimetry of ^{192}Ir sources used in brachytherapy. For all areas mentioned, PTB uses additional water calorimeters to obtain experimental data which ultimately contribute to a reduction in the measurement uncertainties and to quality assurance in dosimetry for radiation therapy.

2 Calorimetric determination of the absorbed dose to water

According to Equation (1), the absorbed dose to water D_W is defined as the quotient from d$\bar{\varepsilon}$ and dm, whereby d$\bar{\varepsilon}$ indicates the mean energy imparted to a mass element dm of the material "water" by ionizing radiation. The unit of this measurand is the gray (Gy). The following applies: 1 Gy = 1 J/kg.

$$D_W = \frac{d\bar{\varepsilon}}{dm} \tag{1}$$

Using a water calorimeter, this measurand is obtained as a first approximation solely from the measurement of the radiation-induced temperature increase, ΔT, at a measurement point within a water phantom, multiplied by the specific heat capacity, c_p, of water. This is expressed through Equation (2).

$$D_W = \Delta T \cdot c_p \cdot \prod k_i \tag{2}$$

The radiation-induced temperature increase ΔT amounts to approx. 0.24 mK per Gy. As a precondition for the precise measurement of this small temperature increase, very good thermal insulation and active temperature stabilization of

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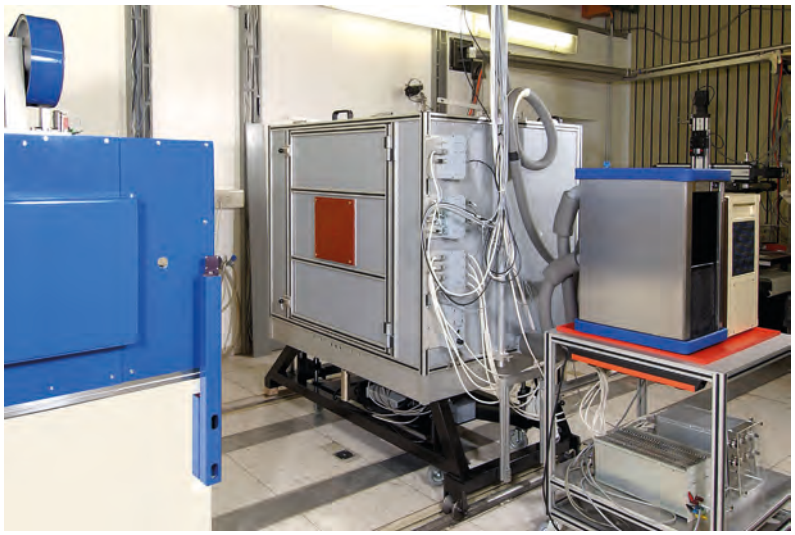

Figure 1: The primary standard water calorimeter in front of PTB's ^{60}Co irradiation facility, including the appurtenant cooling units. The outer enclosure of the calorimeter serves to stabilize the temperature at 4 °C; it has an edge length of approx. 1 m each. The darkly marked square in the centre of the front wall is the radiation entrance window.

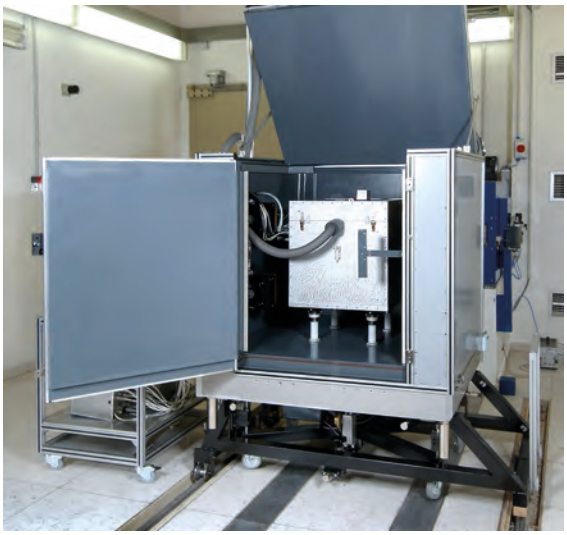

Figure 1a: Photo of the back of the outer enclosure with the cover and the door open. The calorimeter itself is mounted in the centre of the outer enclosure; it consists of the water phantom (including thermal insulation) and of the integrated detector.

the whole calorimeter are required, as the water calorimeter is operated at a water temperature of 4 °C. The calorimeter is operated at 4 °C in order to prevent convection in the water and the – therewith associated – destruction of the radiation-induced temperature distribution at the measurement point.

In addition to the measurement of the radiation-induced temperature increase, the calorimetric determination of D_W also requires, however, the effects of different influence quantities to be taken into account which are summarized in Equation (2) as the product of the corresponding correction factors k_i. For example, perturbation effects of the radiation field, but especially various heat conduction effects or the possible influence of the so-called "heat defect" have to be taken into account and corrected for. Heat conduction effects occur both due to the dissolution of the primary temperature distribution specified by the dose distribution at the measurement point and due to the irradiation of the detector used for temperature measurement (see Section 3), since the materials the detector is made of have specific heat capacities different from water. The heat defect, however, designates the possible difference between the radiant energy absorbed in water and the thermal energy generated in water and is caused by the radiation-induced chain of chemical reactions during the radiolysis of water. If the radiolysis involves additives or impurities dissolved in water, this can cause the release or the absorption of binding energy which can influence the temperature measurement by several percent. The detailed investigation of all the different influence quantities and the determination of the corresponding correction factors represent the main effort when developing a water calorimeter as a primary standard measuring device [1].

3 PTB's water calorimeter

3.1 Basic design

The basic design of the water calorimeters used at PTB is such that it meets the requirements of clinical reference dosimetry. Thus, in a water calorimeter – just like in routine reference dosimetry – a cubical water phantom with an edge length of 30 cm is used; since the water calorimeter is operated at 4 °C, the water phantom is coated with a polystyrene layer of approx. 8 cm thickness. The calorimetric detector can be inserted into the water phantom at different measurement depths relative to the radiation entrance window (e.g. 5 cm in the case of ^{60}Co radiation and 10 cm for high-energy photon radiation). For temperature stabilization, the calorimeter itself is either located inside a larger outer enclosure (with an edge length of approx. 1 m), in which the air temperature is actively adjusted to 4 °C, or it is encased in a "sandwich structure" consisting of insulating material and aluminium plates through which cooling agent flows. The figures below show the different designs of the calorimeters operated at PTB. Figure 1 shows the primary standard water calorimeter in front of the ^{60}Co irradiation facility. The main features shown are the large outer enclosure (with the radiation entrance window darkly marked) and the cooling and supply devices which

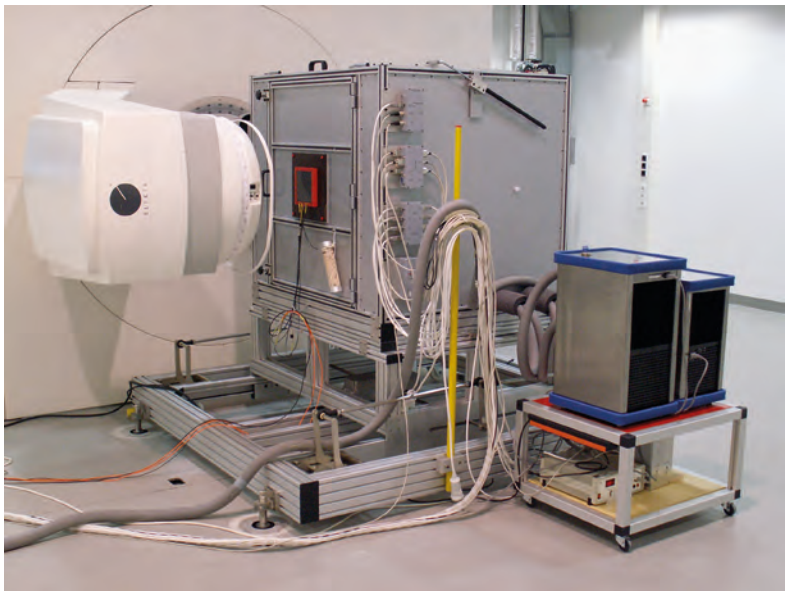

Figure 2: Water calorimeter for high-energy photon radiation in front of the radiation head of PTB's medical linac. The basic set-up of this calorimeter corresponds to the primary standard water calorimeter (see Figure 1).

are necessary to operate the water calorimeter at 4 °C and which ensure a constant air temperature inside the outer enclosure. Figure 1a shows the back of the outer enclosure with the door and the cover open, revealing the calorimeter which is located in the centre of the outer enclosure. A copy of this primary standard water calorimeter is used at PTB's medical accelerators for measurements in high-energy photon fields (Figure 2).

Figure 3, in contrast, shows the so-called "transportable" water calorimeter with the appendant cooling unit. Figure 3a shows the back of the calorimeter, with the cover of the cooling enclosure open. In the case of the – more compact – design of the transportable water calorimeter, temperature stabilization is ensured by means of the above-mentioned "sandwich structure" with cooling plates for active temperature regulation. These cooling plates are placed around the water phantom, on all sides, apart from the aperture of approx. 12 cm × 12 cm for the radiation entrance window. The transportable water calorimeter is particularly well suited for use in external irradiation facilities and was, for example, used at GSI in Darmstadt for measurements with ^{12}C ion beams (raster-scan method).

3.2 Detector

The radiation-induced temperature increase ΔT in water amounts to approximately 0.24 mK per Gy and is measured by means of temperature-calibrated thermistors (Ø: approximately 0.25 mm) which are fused into each tip of thin, tapered glass pipettes (smallest diameter: approximately 0.5 mm, overall length: approx. 110 mm). To be used in the calorimetric detector, two of these temperature sensors have been mounted into a glass cylinder filled with ultrapure water (Ø: 95 mm; h: 41 mm; wall thickness: 0.7 mm and 2.5 mm, respectively), facing each other at a distance of approximately 8 mm (Figure 4). The detector is inserted into the water-filled phantom of the calorimeter at the suitable measurement depth in such a way that the horizontally incident radiation is directed parallel to the cylinder axis. In all water calorimeters used at PTB, the same detector type is used. This geometry and the small wall thicknesses of the glass cylinder and of the temperature sensors, respectively, were chosen to minimize, on the one hand, the perturbation of the radiation field and, on the other hand, to enable the determination of the required correction factors for heat transport

Figure 3: The so-called "portable" water calorimeter with the appurtenant cooler. The temperature of this calorimeter is stabilized by means of actively cooled plates which are placed all around the water phantom, except for the radiation entrance window (framed in red). The edge length of the calorimeter is approx. 60 cm. In the area of the radiation entrance window, the polystyrene insulation layer is approx. 18 cm thick.

Figure 3a: Photo of the back of the portable calorimeter, with the cover of the cooling enclosure open.

effects in the calorimeter with high accuracy by means of finite element calculations.

During an irradiation measurement, the resistance change of approx. 0.18 ohm per thermistor which is associated with the temperature change is determined either by means of a battery-operated DC-voltage resistance bridge circuit or by direct resistance measurement using a precision multimeter. Figure 5 shows the typical measurement signal of the detector over a period of approx. 6 minutes – the actual irradiation takes 120 seconds (start of the irradiation at approx. t = 140 s).

The glass cylinder of the detector contains ultrapure water that has been additionally saturated with nitrogen or hydrogen. Based on detailed experimental investigations combined with numerical simulations with regard to the radiolysis of water, it can be shown that, in this case, the absorbed radiation energy is completely transformed into thermal energy – i.e. there is no "heat defect" [1].

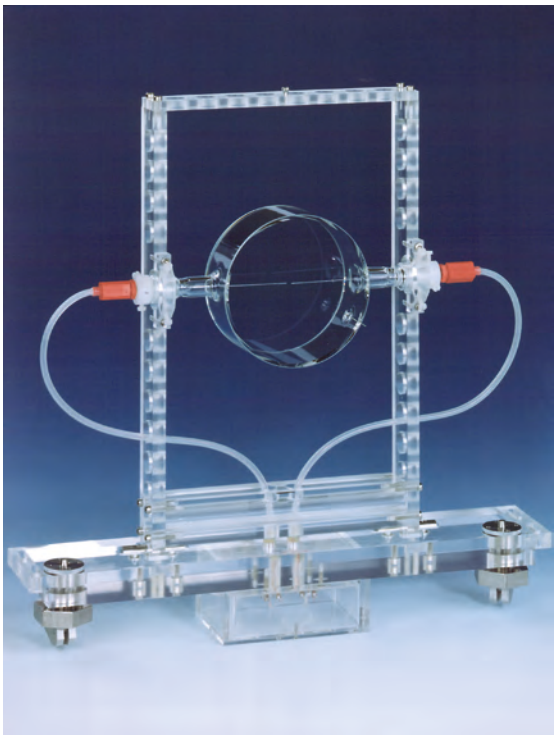

Figure 4: Detector of a water calorimeter. Two temperature sensors are mounted opposite to each other (spacing: approx. 8 mm) inside the glass cylinder which is filled with ultrapure water (Ø: approx. 95 mm, height approx 40 mm). Each temperature sensor consists of a thermistor (Ø: approx. 0.25 mm) which was fused into the tip of a thin glass pipette. The glass pipettes have a total length of approx. 110 mm, and their external diameter at the tip amounts to approx. 0.5 mm.

4 Application example: Determination of k_Q factors for photon radiation

As mentioned in the introduction, k_Q factors of ionization chambers which depend on the radiation quality can be determined experimentally by means of water calorimetry. The k_Q factors are required to take the difference in the response of the ionization chambers between a user-defined radiation quality Q and the reference radiation quality ^{60}Co into account. Thus, k_Q represents the ratio between the D_W calibration factors, N_{Dw}, at the radiation quality Q, and ^{60}Co radiation.

$$k_Q = N_{Dw}^{Q} \Big/ N_{Dw}^{Co} \qquad (3)$$

Using the calorimeter shown in Figure 3, corresponding measurements were carried out at all radiation qualities Q (energy range: 4 MV to 25 MV; field size: 10 cm × 10 cm) available at PTB's medical accelerators. Hereby, each measurement consists of the calorimetric determination of D_W and the subsequent calibration of an ionization chamber directly in the water phantom of the calorimeter, under identical radiation conditions. Figure 6 shows the k_Q factors obtained in this way for three different types of ionization chambers, as a function of the radiation quality (the parameter $TPR_{20,10}$ used in the diagram is a measure of the radiation quality Q). The relative standard measurement uncertainty of the experimental data amounts to approx. 0.3 %. Using these experimentally obtained k_Q factors allows the standard measurement uncertainty occurring in reference dosimetry of high-energy photon radiation to be significantly reduced, since a standard measurement uncertainty three times as high has to be assumed for the calculated k_Q values that have been used to date.

5 Outlook

Water calorimetry is an energy-independent measurement procedure used to determine D_W for dosimetry in radiation therapy. The field of application of water calorimetry extends, as a matter of principle, to all types of radiation and radiation qualities used in radiation therapy as well as to a broad field of different irradiation conditions. PTB therefore operates several water calorimeters – for the reference radiation fields for photon and electron radiation, which are important for dosimetry, for small-dimension radiation fields, and for specific radiation conditions such as, e.g., the raster-scan method for ^{12}C ion beams. More recent developments are aimed at applying water calorimetry directly to determine D_W under IMRT irradiation conditions (IMRT: Intensity Modulated Radiation Therapy), e.g. when smaller fields from different irradiation angles overlap. For this purpose, a water calorimeter with a cylindrical water phantom is being set up.

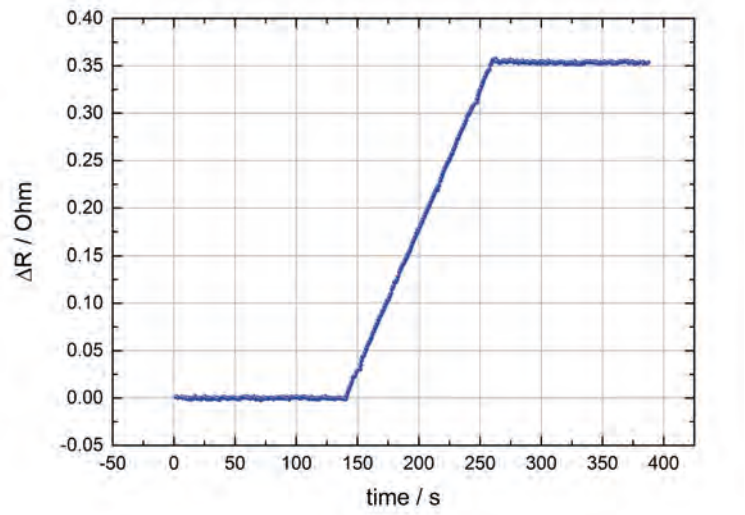

Figure 5: Measuring signal of the detector before, during and after an irradiation of 120 s with ^{60}Co radiation. The radiation is switched on at t = 140 s. The change in resistance is recorded by means of a DC-voltage resistor bridge circuit.

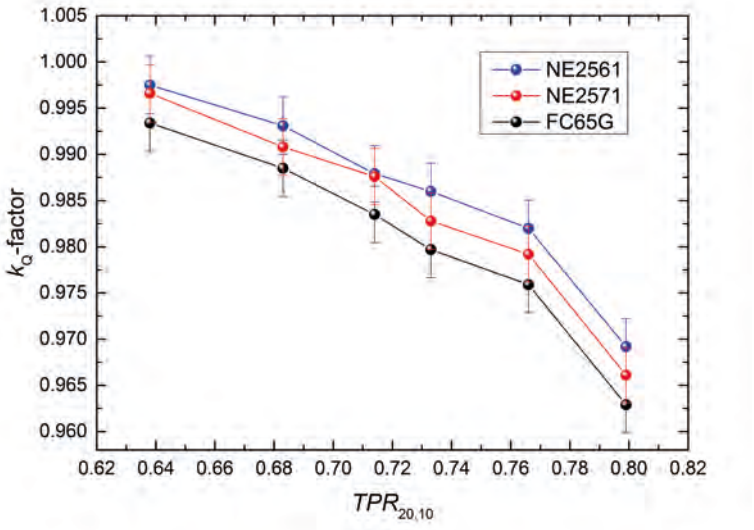

Figure 6: Experimentally determined dependence of the k_Q factors on the radiation quality of the photon radiation for three different types of ionization chambers. The relative standard measurement uncertainty amounts to approx. 0.3 %.

6 Literature

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Dosimetry with Ionization Chambers in External Radiation Therapy

Ralf-Peter Kapsch*

Introduction

The precise irradiation of patients in external radiation therapy is based on the exact knowledge of the dose which is generated by the irradiation facility (this is usually a clinical linac) under standardized conditions – the so-called "reference conditions". This "basic dosimetry" is concretely aimed at determining the absorbed dose to water at a certain point in the water phantom (which serves as a patient replacement). Hereby, only ionization chamber dosemeters are used, as they allow the dose to be measured with very low uncertainty. The exact procedure is described in detail in so-called "dosimetry protocols" such as, e.g., the German standard DIN 6800-2 [1] or the international protocol TRS-398 [2] which was published by IAEA. In the following, the basics of dosimetry with ionization chamber dosemeters will be presented.

Set-up and functioning principle of an ionization chamber dosemeter

The eponymous property of ionizing radiation is the ability to ionize air. Due to interaction processes between the radiation and air molecules, a part of the radiation energy is transferred to the air molecules. Hereby, both positively and negatively charged ions may occur.

An ideal ionization chamber consists of a small air-filled cavity in which an electric field is present. The positively and negatively charged ions generated in the event of an irradiation are separated by the electric field. The total electric charge of the ions having the same sign is measured by means of an electrometer; this charge is a dose measure.

Real ionization chambers contain additional components such as, e.g., electrodes (to generate the electric field and to gather the charges), a chamber wall to enclose the air-filled measuring volume, a stem to fix the chamber, electric wire for the connection to the electrometer, etc. (see Fig. 1).

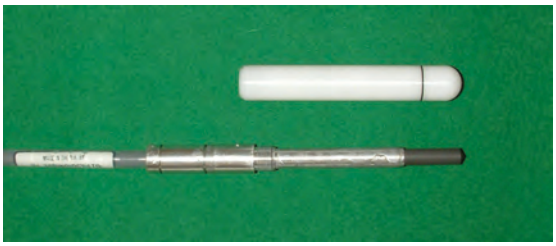

Figure 1: A typical ionization chamber as used in external beam therapy (bottom) with protection sleeve (top). The air-filled cavity is located inside the black graphite cylinder which is visible on the right-hand side and has a diameter of 7 mm and a length of 24 mm. The wall of this hollow graphite cylinder has a thickness of only 0.36 mm and serves as one of the two electrodes for the generation of the electric field. The second electrode is located inside the air cavity and is not visible from the outside.

Determining the dose by means of ionization chamber dosemeters

The mean absorbed dose to air inside the collecting volume of an ideal ionization chamber $\bar{D}_{\mathrm{air}}$ is given by the quotient from the radiation energy absorbed in this air volume $\varepsilon_{\mathrm{air}}$ and the mass of the air volume m_{air}:

$$\bar{D}_{\mathrm{air}} = \frac{\varepsilon_{\mathrm{air}}}{m_{\mathrm{air}}} \qquad (1)$$

The radiation energy absorbed in the air volume of the ionization chamber can be expressed as the product of the number of ion pairs generated and of the mean energy W_{air} which is necessary to generate one ion pair in air (see Fig. 2).

The number of ion pairs generated can be determined from the electric charge of the ions having the same sign which is measured by means of an electrometer. Since these are single-charge ions, the total charge Q is the product of the number of ions and of the elementary charge e.

All in all, the mean absorbed dose to air in the collecting volume of the ionization chamber can be calculated from the measured electric charge:

$$\bar{D}_{\mathrm{air}} = Q \cdot \frac{W_{\mathrm{air}}}{e \cdot m_{\mathrm{air}}}. \qquad (2)$$

For reference basic dosimetry in external beam

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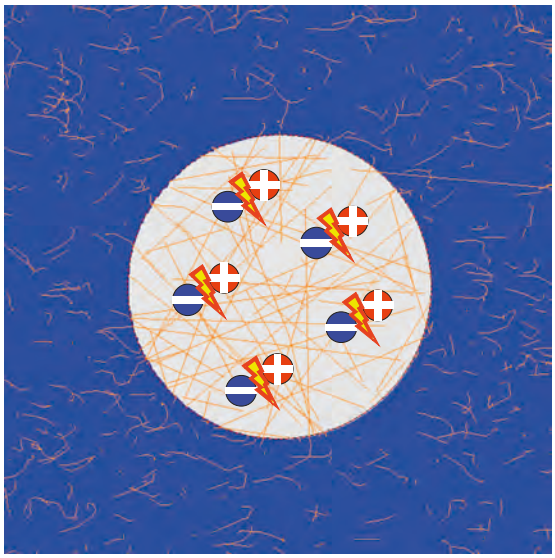

Figure 2: Schematic representation of an ideal ionization chamber (small air bubble) in a water phantom. The orange lines represent the trajectories of the secondary electrons generated during the irradiation. Interactions of these secondary electrons with the air molecules lead to the formation of positively and negatively charged ions. In each of these ionization processes, on average the energy W_{air} is transferred.

therapy, however, not the mean absorbed dose to air in the ionization chamber is generally of interest, but the absorbed dose to water at a certain point in the water phantom. Under the assumption that the ionization chamber complies with the so-called "Bragg-Gray conditions" (which mainly means that the presence of the ionization chamber does not perturb the radiation field in the water phantom[1]), the mean absorbed dose to air $\bar{D}_{air}$ inside the measuring volume of the ionization chamber can then be converted into the absorbed dose to water $D_W(P)$ at a point P in the undisturbed water phantom:

$$D_w(P) = \bar{D}_{air} \cdot s_{w/a} = Q \cdot \frac{W_{air}}{e \cdot m_{air}} \cdot s_{w/a}. \qquad (3)$$

The conversion factor $s_{w/a}$ is the ratio of the mass collision stopping power (cf. [3] for example) of water and air, which depends on the type and on the energy of the radiation.

When using real ionization chambers (see Fig. 1), the Bragg-Gray conditions can be fulfilled only approximately, since the finite dimension of the air volume or the presence of the chamber wall, of the stem and of the electrode, for example, can perturb the radiation field in the water phantom. In practice, these deviations from the ideal conditions are taken into account by means of perturbation factors p which correct for the perturbations due to the chamber wall (p_{wall}), to the electrode (p_{cel}) or to the finite dimensions of the measuring volume (p_{cav} and p_{dis}). When using a real ionization chamber, the determination of the absorbed dose to water from the electric charge thus requires the following relation to be used:

$$D_w(P) = Q \cdot \frac{W_{air}}{e \cdot m_{air}} \cdot s_{w/a} \cdot p_{wall} \cdot p_{cel} \cdot p_{cav} \cdot p_{dis}. \qquad (4)$$

The values of the perturbation factors occurring in this equation depend on the type and on the energy of the radiation as well as on the exact set-up and on the materials used for the ionization chamber. They can, in general, only be determined by means of complex experiments or Monte Carlo numerical simulations. Since it is, in addition, difficult to determine the mass of air present in the collecting volume of the ionization chamber (m_{air}) with a sufficiently small measurement uncertainty, Eq. (4) is *not applied directly* in routine dose measurements in radiotherapy clinics and hospitals.

The relation between the absorbed dose to water D_w and the electric charge Q is determined experimentally instead. If all the quantities occurring on the right-hand side of Eq. (4) – apart from the electric charge Q – are summarized to form a proportionality factor N, the following simple relation is yielded:

$$D_w(P) = Q \cdot N. \qquad (5)$$

The proportionality factor N, which – under certain conditions (see below) – is also called "calibration factor", is determined experimentally for each single ionization chamber in calibration laboratories. The pre-condition for calibration is that the absorbed dose to water $D_W(P)$ is known under certain conditions. At PTB, a primary standard, the water calorimeter, is used to measure the absorbed dose to water.

The values of the parameters occurring in Eq. (4) – and thus also the value of the proportionality factor N – are influenced by a multitude of influence quantities. These are, for example, the type and the spectrum of the radiation which influence the stopping power ratio and the perturbation factors; the temperature and the air pressure which influence the mass of the air present in the ionization chamber; the humidity which influences the value of the parameter W_{air}; or the electric field strength inside the ionization chamber which influences the charge collected at the electrodes[2], etc. For this reason, so-called "reference conditions" to which the calibration factor N applies are defined in the dosimetry protocols [1][2]. For dose measurements under reference conditions, Eq. (5) can then be applied if the calibration factor is known.

In practice, however, the absorbed dose to water often has to be measured under conditions which deviate from the reference conditions. Typical cases are, for example, measurements in the photon beam of a clinical linac whose spectrum deviates from the ^{60}Co spectrum which is normally used for calibration, or measurements at an air pressure different from the reference value 101.325 kPa. In such cases, Eq. (5) cannot be used without further ado, since the calibration factor N determined under reference conditions is not valid

[1] For an exact definition of the Bragg-Gray conditions, please cf. [3], for example.

[2] If the positive and negative ions formed during the irradiation are not separated "fast enough" in the electric field, they can re-combine with each other and are then not detected when the charge is measured.

as the proportionality factor under measuring conditions deviating from the reference conditions. Similar to the procedure to take the deviation from the Bragg-Gray conditions into account, the deviations of the measuring conditions from the reference conditions are taken into account by several correction factors k_i. The equation usually used to determine the absorbed dose to water with ionization chambers thus reads:

$$D_{\mathrm{w}}(P) = Q \cdot N \cdot k_{\mathrm{P}} \cdot k_{\mathrm{S}} \cdot k_{\rho} \cdot k_{\mathrm{h}} \cdot k_{\mathrm{Q}} \cdot k_{\mathrm{NR}}. \qquad (6)$$

The meaning of the correction factors occurring here is explained in the dosimetry protocols [1][2]. Contrary to the perturbation factors p occurring in Eq. (4), the correction factors k_i can often be determined more easily, since they only describe small, relative changes in the measured value (as a function of the value under the reference value). The methods and data used to determine the correction factors occurring in Eq. (6) are described in detail in the dosimetry protocols [1][2].

Equation (6) is used for dose measurements in external beam therapy under various measurement conditions and with a multitude of different ionization chamber dosemeters. Due to the use of a modern primary standard (the water calorimeter) for the calibration of ionization chambers and for the determination of the correction factor k_Q, it has now become possible to determine the absorbed dose to water with a relative standard measurement uncertainty of approx. 1 % in clinical routine.

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[2] International Atomic Energy Agency: Absorbed Dose Determination in External Beam Radiotherapy. An International Code of Practice for Dosimetry Based on Standards of Absorbed Dose to Water. Technical Reports Series No. 398, IAEA, Vienna, 2000

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Alanine Dosimetry

Mathias Anton*

Objective

In modern radiotherapy, modalities such as in the so-called *intensity modulated radiotherapy* (IMRT) or in tomotherapy, a dose distribution is generated the contours of which are to be as close to the target volume (such as the tumor tissue) as possible. Such a distribution is produced by a superposition of many fields, which are irradiated with different cross-sectional dimensions and shapes, and from different directions. The fields may be very small; particularly in tomotherapy, individual fields are only 5 mm wide. Conventional dosimeters such as ionization chambers are calibrated in fields that are much larger, typically 10 cm × 10 cm. The response of the dosimeter may, for the small fields, be significantly different from its value at calibration. Therefore, a dosimeter with the following properties would be highly desirable: a weak dependence of the response on the radiation quality (the latter changes slightly with the field size), small, and – due to its material properties – with a minimal field disturbance.

The objective to specify the dose in the target tissue with an uncertainty of less than 2.5 %, issued by the ICRU already in the seventies, is today often not even achieved for conventional radiotherapy. With an ideal dosimeter, the entire dosimetric chain could be checked, also for the modern forms of therapy. The properties of the alanine dosimeter come quite close to the ideal.

Alanine

Alanine is an amino acid. Its chemical components are similar to those of proteins. Alanine is present in crystalline form. Ionizing radiation produces free radicals in these crystals, which are stably bound. With the help of an electron spin resonance spectrometer (ESR), the number of radicals can be relatively determined. The concentration of free radicals, i.e. the number of radicals per mass of the irradiated alanine, is proportional to the absorbed dose.

Alanine can be processed with various binders to detectors in various forms. PTB uses mainly alanine pellets produced by the Harwell company. These were developed at the NPL and have been marketed by Harwell for several years. They consist of about 91 % of L_α alanine (microcrystalline) and 9 % of paraffin as a binder.

With a diameter of 4.9 mm and a height of 3 mm, the tablets have a weight of 60 mg. The density is about 1.2 g/cm^3, the effective atomic number Z_{eff} = 7.2. These parameters, which are essential for the radiation transport properties, are

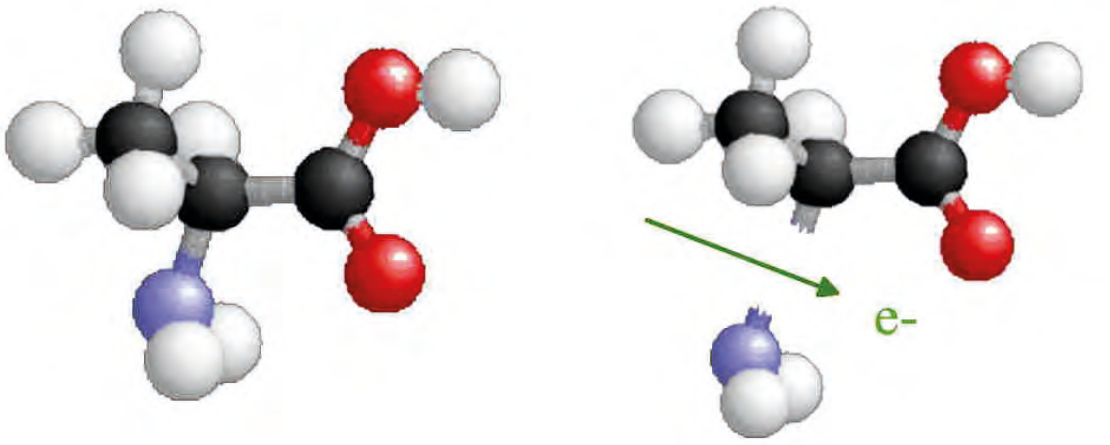

Figure 1: Left: Molecular model of alanine. Black: carbon, white: hydrogen, red: oxygen, blue: nitrogen. Right: Simplified presentation of the formation of free radicals – the amino group is separated by the incident radiation.

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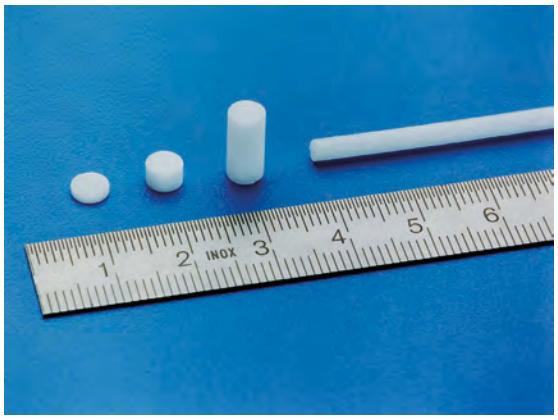


Figure 2: Various forms of alanine detectors: tablets or (on the right) extruded strands are available.

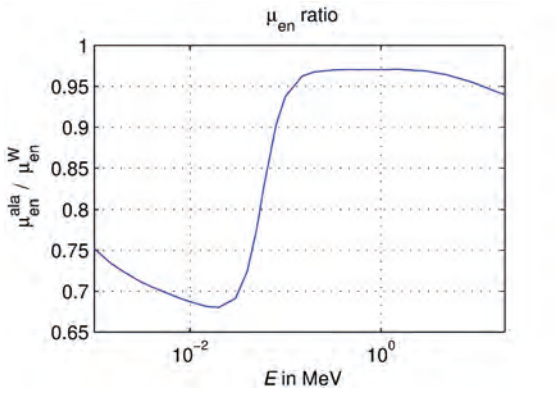


Figure 3: An essential parameter for the radiation transport is μ_{en} / ρ, the mass energy absorption coefficient. The figure shows the ratio of these coefficients for alanine and water. In particular, in the (therapy-related) range around 1 MeV, the ratio is almost constant.

quite close to those of water. This is of advantage because the relevant quantity for radiation therapy is the absorbed dose to water.

Electron Spin Resonance Spectroscopy (ESR)

The energy difference of the two possible spin states of a free electron in a magnetic field of flux density B_o is given by

$$\Delta E = \mu_B \cdot g \cdot B_o.$$

Here, μ_B is the Bohr magneton, and g is the Landé factor (for a free electron, g is almost exactly equal to 2). Absorption of electromagnetic radiation at the resonant frequency $f = \Delta E/h$ induces transitions from the lower to the higher energy level. This can be expressed as $f = 2.8026 \cdot 10^{10} \cdot B_o$ Hz/T, i.e. a magnetic field around 0.35 T corresponds to a resonance frequency in the so-called X-band (microwave) around 9 GHz to 10 GHz.

By different interaction processes, the population of the higher level is reduced again, i.e. the absorbed energy is dissipated into the environment as heat. For the detection of the resonance, the magnetic flux density is varied linearly and slowly around the resonance value, and the resulting absorption line is registered.

The population difference between the higher and the lower state is very small at room temperature, therefore the absorption signal is also very small. By an additional variation (wobble) of the magnetic flux density with a typical frequency of 100 kHz in addition to the slow variation, the weak signal can be successfully registered by phase-sensitive detection (lock-in amplifier). Therefore, typical ESR signals do not exhibit the typical features of absorption curves, but are rather dispersion curves.

The presence of several hydrogen atoms in the immediate vicinity of the free radical in alanine leads to a hyperfine splitting of the resonance.

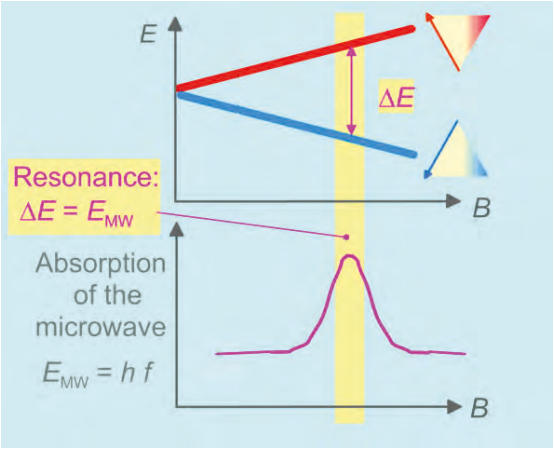


Figure 4: Schematic representation of the electron spin resonance. If the energy difference between the two spin-states matches the energy of the incident microwave, a maximum of the absorption results.

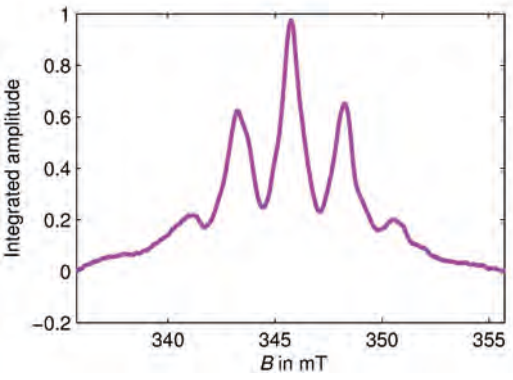


Figure 5: By numerical integration of the dispersion curve recorded by the ESR spectrometer, the absorption curve is obtained. The five hyperfinestructure lines of alanine are visible.

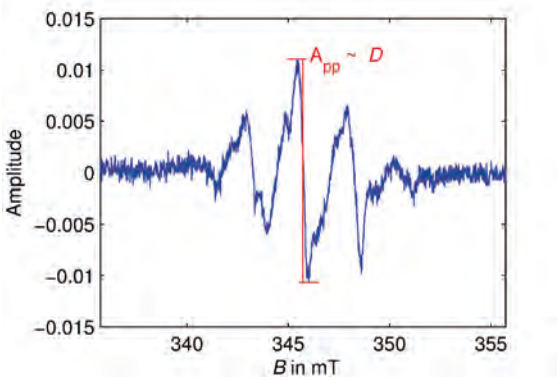


Figure 6: An ESR signal of alanine obtained with a modulation frequency of 100 kHz and a modulation amplitude of 0.1 mT is displayed. The peak-to-peak amplitude App is proportional to the number of detected radicals.

Figure 7: Probe with a PE shrink-wrapped detector.

Apparatus

One up to four alanine pellets constitute one detector. The dosimeter probe consists of a detector and a waterproof sheath. Usually, a holder made of perspex (PMMA) is used which fits into a waterproof sheath matching a special ionization-chamber type. The detector may also be shrink-wrapped in polyethylene foil (PE). During irradiation, usually in a water phantom, the temperature of the probe needs to be registered.

The ESR spectrometer, a Bruker EMX 1327, is situated in an air-conditioned laboratory room. For the measurements, a highly sensitive resonator is used. During the ESR measurement, the temperatures of the air and of the cooling water of the magnet as well as the humidity of the ambient air are recorded.

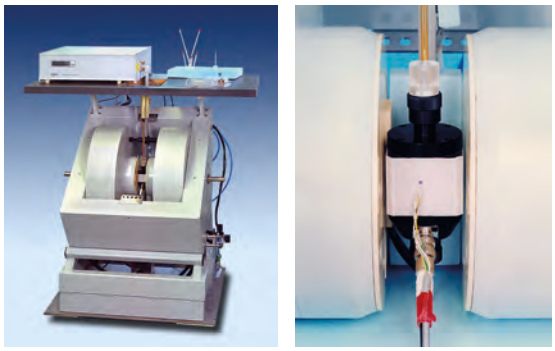


Figure 8: Left: Bruker EMX 1327 ESR spectrometer. Right: High-sensitivity resonator

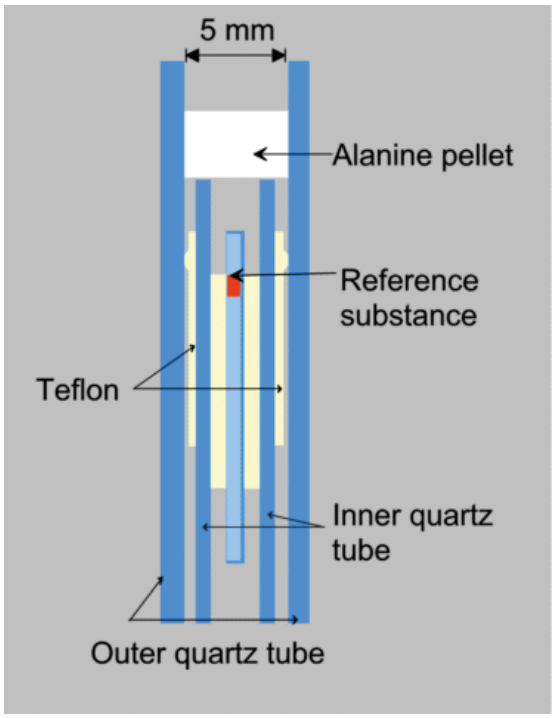


Figure 9: Schematic representation of the positioning device for the alanine pellet and the reference substance within the resonator.

The device for positioning the pellets in the resonator was made at PTB. It also contains a reference substance provided by Bruker. The simultaneous measurement of the alanine and the reference makes it possible to compensate for variations in the sensitivity of the spectrometer.
The mass of each individual pellet is determined by a microbalance MX-5 (Mettler). The pellets are handled by vacuum tweezers only.

Signal processing

For each alanine pellet, 5 spectra are recorded. Between the measurements of the individual spectra, the pellet is rotated by 72°. By the subsequent averaging of the amplitudes, positioning uncertainties which are due to unavoidable mechanical tolerances can be compensated for.

The measurement of the concentration of radicals is not absolute, the amplitudes are therefore not only determined relative to the reference substance, but also relative to amplitudes of pellets which were irradiated with a known dose (usually 25 Gy) in the ^{60}Co reference field of PTB. From the spectra of 4 pellets irradiated with 25 Gy and of 4 unexposed pellets, two spectra are produced by subtraction. One of these represents a pure alanine spectrum, the other one is a spectrum of an unirradiated tablet, combined with the spectrum of the reference substance. These so-called base functions are determined on each day of measurement and are fitted to the measured spectra by a least-squares method. Thus, the amplitude determined is relative to ^{60}Co-irradiated tablets, whereby a daily calibration of the spectrometer is achieved. At particularly high demands on the accuracy, a calibration curve can be generated from a number of further ^{60}Co-irradiated tablets with different doses which are measured in addition.
The measurement is time-consuming. For each pellet, 10 minutes are required for handling and measurement. The analysis using fitting of the experimentally determined base functions is more accurate than the widely used evaluation of the peak-to-peak amplitude.

Uncertainties

The usable measuring range of PTB's secondary standard measurement system is between 2 Gy and 25 Gy. The measurement uncertainty increases with decreasing dose.

The largest contributions to the uncertainty budget result from the ESR amplitude determination. For a single pellet, the uncertainty

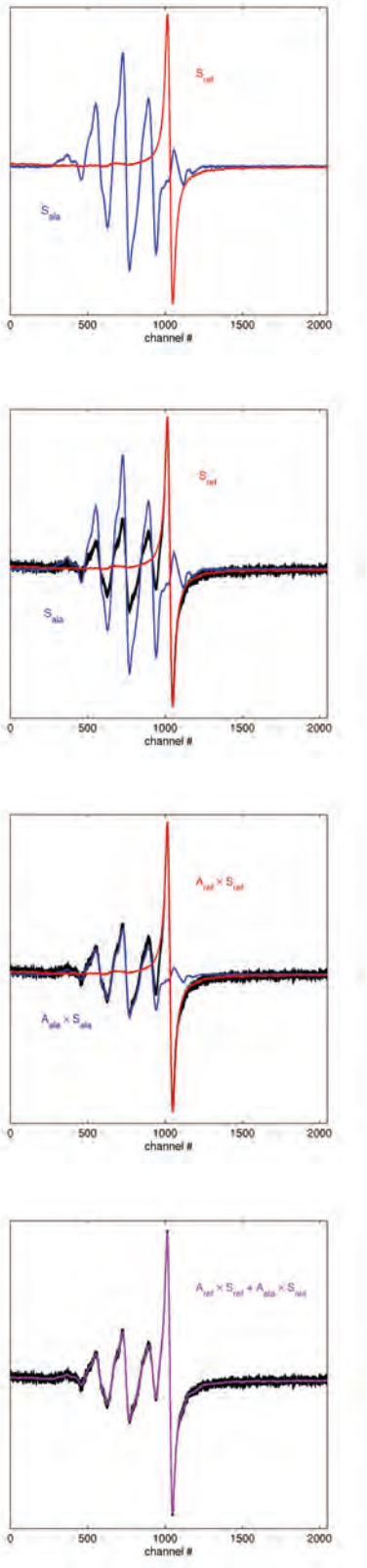


Figure 10: Schematic representation of the signal processing. The base functions for alanine (blue, S_{ala}) and for the reference substance (red, S_{ref}) are fitted to the signal to be evaluated (shown here in black). The fit coefficients are A_{ala} and A_{ref}. The mass-normalized ratio A_{ala}/A_{ref} is used as the measurand for the concentration of free radicals, which is proportional to the absorbed dose.

component from the amplitude measurement repeatability is equivalent to about 40 mGy. A further contribution comes from the (inevitable) background signal of 20 mGy. In the mentioned range, these two components are independent of the dose. Another contribution of about 0.3 % to 0.4 % results from variations in the composition of the pellets. The combined uncertainty can be reduced, by averaging over n pellets, to $1/\sqrt{n}$ times the contribution of a single tablet. Smaller contributions to the overall uncertainty result from the uncertainty of the mass, the temperature during irradiation and, if a longer time between irradiation and ESR analysis passes, from the so-called *fading*. Fading is the loss of free radicals with increasing time. The loss depends strongly on the temperature and the humidity. However, in a laboratory under constant conditions (relative humidity below 50 %, temperature 22.5 ° C), this loss is not greater than 2.5 % per year. Thanks to the measurement method used at PTB, this influence can be neglected, as long as the pellets that are used for calibration and the ones to be examined are stored under the same conditions, and as long as there was no long delay between the irradiation of the calibration- and the test-pellets. Usually, four pellets per dose are irradiated and analysed. Under these conditions, a relative standard uncertainty of 0.35 % is obtained for a dose of 10 Gy (using a calibration only by the base function). For 2 Gy under the same conditions, 1.1 % result; for 20 Gy, only 0.28 % are obtained. Here, the uncertainty of 0.20 % of the primary standard is not included. The achieved uncertainties are thus sufficiently small to ensure that alanine can be used effectively for the intended objectives.

Response

The qualities most often used in radiotherapy are ultra hard X-rays that are generated in accelera-

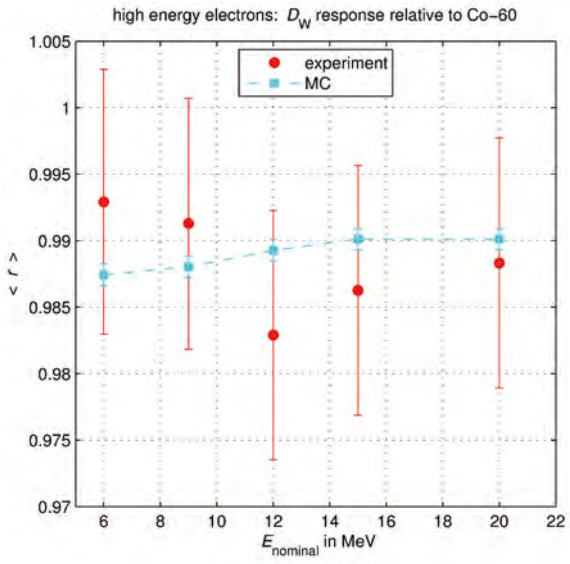


Figure 11: Relative response of the alanine dosimeter with respect to the absorbed dose, relative to Co-60, as a function of the nominal energy (accelerating voltage) for high-energy electrons. Red: experimental data; cyan: Monte Carlo simulation results.

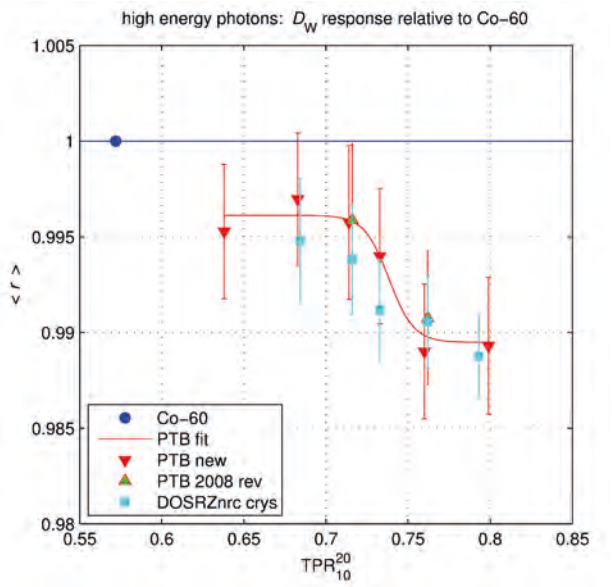


Figure 12: Relative response of the alanine dosimeter with respect to the absorbed dose, relative to Co-60, as a function of the tissue-phantom ratio TPR. Triangles: experimental results, the lowest value of TPR is equivalent to 4 MV X-rays, the highest corresponds to 25 MV; blue: reference Co-60; cyan: Monte Carlo simulation results.

tors with accelerating voltages of up to 25 MV. The qualities are therefore often referred to briefly as 25 MVX, 10 MVX, etc. Irradiations by electrons with energies in the MeV range are also widely used in radiotherapy. For the reference field size of 10 cm × 10 cm, the response of the alanine dosimeter for MV X-rays and for MeV electrons was determined (the latter in cooperation with the Swiss Metrology Institute METAS), relative to the response for ^{60}Co radiation. With increasing energy, the relative response for X-ray radiation decreases from 0.996 for 4 MV to 0.989 for 25 MV. The relative response for 25 MV is almost identical to that for electron beams with energies between 6 MeV and 20 MeV, which seems to be energy-independent. These data are consistent with data from Monte Carlo simulations, whereby the so-called *density correction* must be applied for the density of crystalline alanine, not for the bulk density of the alanine pellets. This can be explained by the fact that the interactions that lead to the formation of radicals take place within the micro-crystals with a density of about 1.4 g/cm^3.

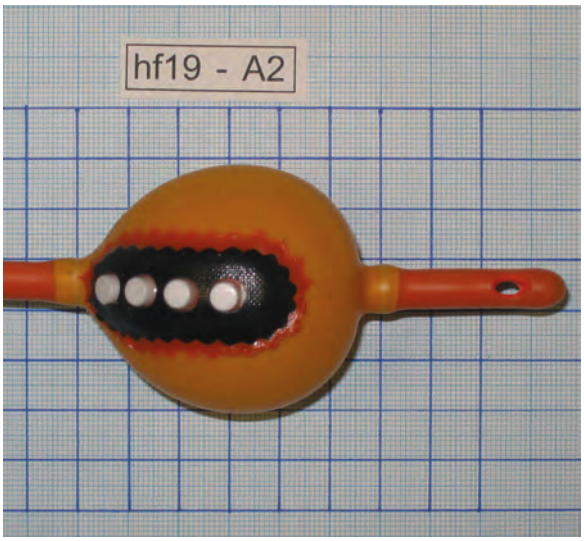
Applications

In cooperation with the University Hospital Göttingen, dose measurements were carried out in patients and anthropomorphic phantoms. In teletherapy of prostate cancer it was demonstrated that the use of an air-filled rectal balloon does not lead to an undesired change of the dose in the target volume. By using such a balloon, the intestinal wall is pushed away from the prostate, in order to be moved out of the radiation field and thus to prevent inflammation due to excessive irradiation.

In brachytherapy of prostate cancer with ^{192}Ir emitters, measurements were performed within the urethra. The measurements were intended to demonstrate that the sparing of the urethra, which is a so-called organ at risk, is actually achieved as planned. For this purpose, a special probe with modified dimensions was developed and investigated. Measurements on a phantom were very successful. In the in-vivo measurements, problems with the positioning of the measuring probes were believed to be responsible for the differences observed.

Further measurements were carried out at irradiations in the head and neck region, to quantify the sparing of organs at risk which can be achieved by using a mouth wedge.

A copy of PTB's measurement system (hardware and software) was set up by cooperation partners in Belgium and was successfully used for nationwide quality assurance measurements in therapy centres. The results of the audit were published by Schaeken et al. (2011).



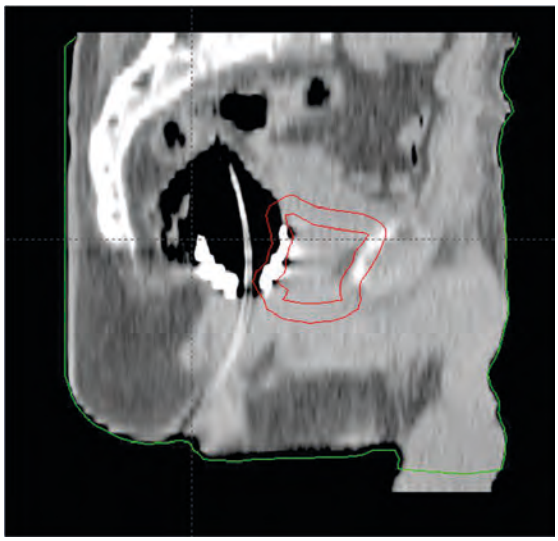


Figure 13: Measurements using a rectal balloon. Left: Alanine pellets shrink-wrapped in polyethylene film on a rectal balloon. Right: Positioning of alanine detectors, computer-tomographic image.

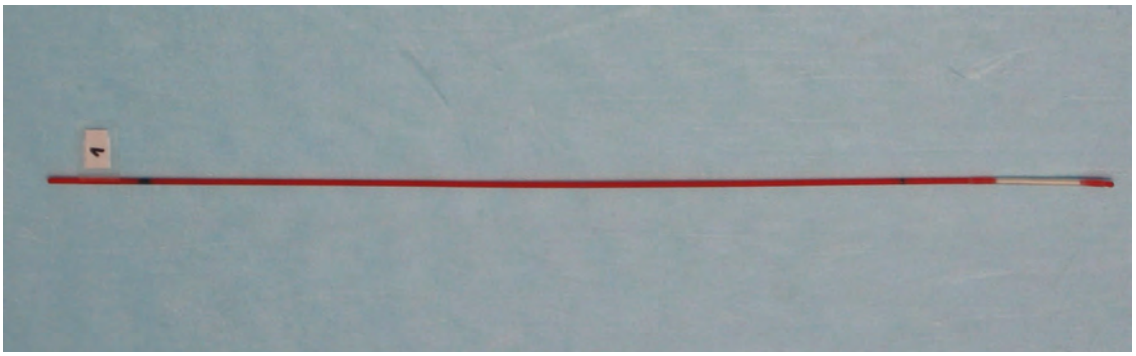


Figure 14: A specially developed probe for measurements within the urethra. In this case, alanine is not irradiated as a pellet but as a powder. Tabletting is carried out after the irradiation. The diameter of the probe is about 2.5 mm.

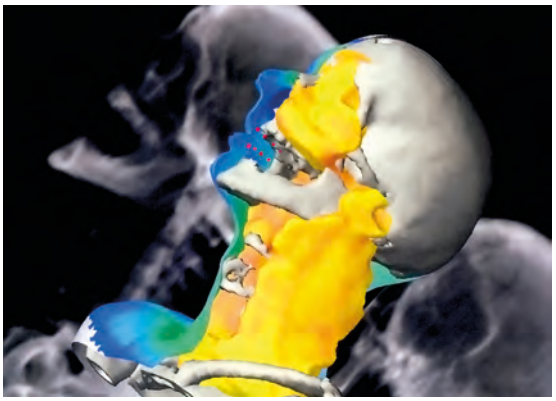


Figure 15: CT image showing a patient with a wedge (not visible) equipped with alanine pellets. The latter are shown as red dots.

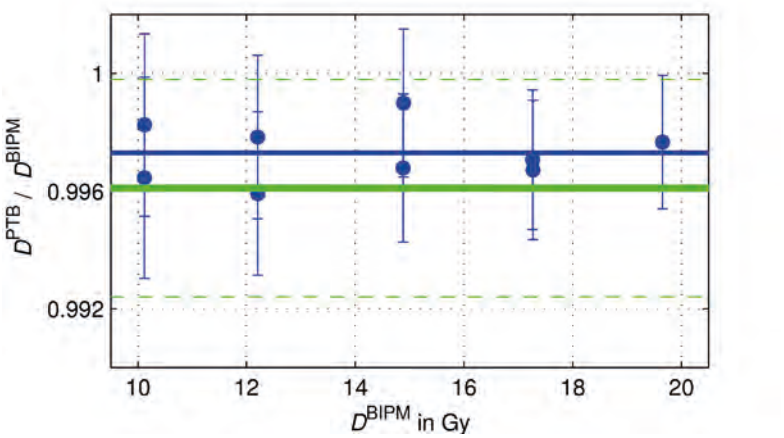


Figure 16: Results of the blind test with the BIPM: the blue dots represent the ratio of the determined dose to the delivered dose as a function of the delivered dose. The error bars represent the uncertainty contribution of the alanine dosimetry system. The green solid line represents the ratio of primary standards; the dashed lines represent the standard uncertainty of this ratio.

Intercomparisons

In 2010, the British National Physical Laboratory (NPL), the French national metrology institute (LNE LNHB) and PTB compared their alanine dosimetry systems for Co-60 and for high-energy X-rays. Information on this can be found on the website of the BIPM (EURAMET.RI(I)-S7).

In addition, PTB was subjected to a blind test, conducted by the BIPM. Alanine dosimeter probes were irradiated at the BIPM, but the dose was revealed only after evaluation by PTB. The test results are very satisfactory, taking into account the known difference in the primary standards (EUROMET.RI(I)-K4): there is a difference between the determined and the applied dose of about 0.1 %.

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(selection)

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Further influence quantities

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(application example: determination of the temperature coefficient / irradiation temperature alanine)

Applications

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Schaeken, R. Cuypers, S. Lelie, W. Schroeyers, S. Schreurs, H. Janssens and D. Verellen in Radiotherapy and Oncology **99**, 1 (2011), pp. 94–96

Radiation Protection in Medicine

Peter Ambrosi*

Radiation protection – for whom?

When working with radioactive substances or applying ionizing radiation, people can become exposed to these substances or this radiation. It is the task of radiation protection to keep this exposure as low as possible. Radiation protection in medicine addresses three different groups: hospital staff, patients, and assisting persons.

The **hospital staff** belong – if they have to work with ionizing radiation – to those persons who are occupationally exposed to radiation, as they can be exposed to radiation when doing their job. Typical fields of work in diagnostics include the application of X-radiation (see Figure 1 in this article) or of radioactive substances, e.g. in nuclear medicine (see Figure 1 of the article "Partial-body Dosimetry for Photon and for Beta Radiation" in this publication). Typical fields of work for treatment include the use of accelerators, e.g. in radiotherapy, or treatment with radioactive substances.

For a **patient**, a distinction can be made between his/her target organ (target volume) to be examined or to be treated, and the radiation exposure of the remaining body. For the target volume, the treatment with ionizing radiation is justified by the chance of a diagnosis which could not be obtained otherwise, or of healing, from which the patient then benefits. This does not apply to the other organs of the patient which surround the target volume. Their irradiation must be kept as low as possible. This is the task of the hospital staff who are responsible for diagnostics and radiation therapy.

Figure 1: X-ray examination with a C bend. The lead apron which is usually worn was not put on for this photo.

The **assisting persons** support the patients in the medical applications of ionizing radiation. However, they do not benefit from the diagnostics or therapy themselves. Examples are assisting parents who calm down their children, thereby making X-raying possible at all, or assisting relatives who support the medical personnel in attending elderly patients or patients suffering from dementia.

Dose limits

As the hospital personnel is occupationally exposed to radiation, it is subject to special provisions which are described in more detail in the article "Official Personal Dosimetry for Medical Staff" in this publication. For persons who are occupationally exposed to radiation, higher dose limits apply than for the population in general. For comparison: the annual limit for the effective dose is 20 mSv for persons who are occupationally exposed to radiation, and 1 mSv for the general population. In comparison, the mean annual dose due to natural ambient radiation, e.g. from space and from the soil, amounts to approximately 3 mSv in Germany. All dose limits apply to radiation in addition to this natural radiation component. The terms defining a dose, e.g. the effective dose, are explained in the article "Measurands in Radiation Protection" in this publication. (Note on translation: The latter article describes the terms according to the new draft of the respective standards, whereas in the other articles in this publication, the English terms are utilized as they are currently in use.)

The same dose limits per year as to men apply to women who are occupationally exposed to radiation and are not pregnant. One exception applies to the uterus. In the case of pregnant women, the foetus is always classed as belonging to the **population**, even if the mother is grouped into **persons who are occupationally exposed to radiation**. Thus, the dose limit of 1 mSv applies to the foetus from the point in time where the pregnancy has been announced, until the end of the pregnancy. The staff members occupationally exposed to radiation must wear official personal dosemeters (whole-body dosemeters and, if applicable, finger-

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ring dosemeters) for the measurement of the personal dose (see the article "Measuring Instruments and Challenges in Radiation Protection Metrology" in this publication) and are entitled to wear a further, direct-reading (electronic) dosemeter to measure and check the personal dose themselves. For the patients, no dose limits exist, and they do not wear dosemeters.

Exposure during therapy and diagnostics

In radiation therapy using accelerators, the doses applied to the patient are much higher than the dose limits. This becomes immediately comprehensible if you take into account that the doses are applied to kill the irradiated tumour tissue, whereas the dose limits are to ensure that the person will not suffer any health detriment. For this reason, the irradiation rooms are secured by means of various measures preventing medical staff or other (assisting) persons apart from the patient from being present in the room. Also outside the direct beam, the dose rate due to the indirect scattered radiation is so high that staying in the room for a few hours may be sufficient to exceed the annual dose limit of the effective dose of 20 mSv. The other organs of the patient are also exposed to this indirect radiation during radiation therapy. If the indirect radiation dose is too high, new tumours – also known as secondary tumours – may emerge. For further information on the measurement of the scattered radiation in the room, please refer to the article "Measurement of the Radiation in the Accelerator Therapy Room" in this publication. Constructional and technical radiation protection as well as standard working regulations make sure that the hospital staff will not be exposed to radiation during X-ray examinations. However, exemptions are possible, e.g. for the assisting persons in the X-ray room. It would be desirable for these situations if the radiation exposure could be measured by means of a direct-reading (electronic) dosemeter. The X-rays for diagnostics consist of a very short radiation pulse which is much shorter than a second. This avoids motion unsharpness in the photos, e.g. when the patient is moving, or due to his heartbeat. These short radiation pulses of typically ten milliseconds require special measures for the design and testing of electronic personal dosemeters, which will be described in the article "Electronic Dosemeters for Pulsed Radiation" in this publication.

X-radiation, however, is also applied parallel to surgery, e.g. in angiography, if a catheter is to be led through the blood vessels to the heart. Here, the actual position of the catheter is shown by means of pulsed X-rays. During this surgery, all members of the surgery team are exposed to the scattered radiation of the patient. This exposure can be reduced by means of shielding. It is, however, not completely avoidable. Furthermore, the surgeon runs the risk of parts of his hands and arms coming directly into the X-ray beam. Therefore, a partial-body dosemeter must be used in addition to the whole-body dosemeter. The technical properties of partial-body dosemeters will be outlined in the article "Partial-body Dosimetry for Photon and for Beta Radiation" in this publication.

For the assisting persons, the possible exposure conditions can be simulated very well. Therefore, the potential dose values can be measured in advance (see the article "Dose for Assisting Persons in Human Medicine, Dentistry and Veterinary Medicine" in this publication).

Handling of radioactive substances

Therapy and diagnostics in the field of nuclear medicine also imply the handling of radioactive substances. Hospital staff cannot avoid the handling of these substances, e.g. when it comes to measuring the prescribed activity amount, when preparing a syringe, when injecting the patient, and also for diagnostics during a subsequent measurement on the patient. From the perspective of radiation protection, a distinction must be made between two different ways of radiation exposure. First, the ionizing radiation developing during the decay of the radionuclides can affect the personnel from outside through the walls of the transportation vessel, of the syringe or from inside the patient, which is what you call "external exposure". When handling radioactive substances, this external exposure mostly concerns the hands. Thus, it is measured by means of a partial-body dosemeter (see the article "Partial-body Dosimetry for Photon and for Beta Radiation" in this publication). The second way of exposure is that – when handling the radioactive substance – parts of it can get into the human body (incorporation), e.g. due to inhalation or contact with the skin. This is called "internal exposure", as the radionuclide decays in the body's interior and irradiates the organs from the interior. Internal exposure is hardly measurable. It can, however, be estimated via external measurements of the patient or via measurements of excrement, and via subsequent calculations. However, it can be avoided by working carefully, and will not be further taken into account in this article.

Measuring Instruments and Challenges in Radiation Protection Metrology

Oliver Hupe*

Detectors for ionizing radiation

Ionizing radiation – just like UV radiation – cannot be directly perceived by human beings. However, it can be metrologically determined by exploiting the ionizing effect. If ionizing radiation hits matter, charge carriers are generated which can then be measured. It was this impact which made Wilhelm Conrad Röntgen discover X-radiation in 1895. Here, these unknown "X-rays" blackened films, as had already been known from visible light. In the following, we will briefly present some detectors intended for the detection of ionizing radiation, as well as their underlying measuring principles.

Ionization chambers (as can be seen, e.g., in Figure 1) are mainly used in calibration laboratories and, thus, also at PTB. Due to radiation, air molecules are ionized (see Figure 2), and the generated charge carriers (molecule ions and electrons) are a measure of the dose. The charge carriers are collected on electrodes by means of an acceleration voltage and can then be measured. In a 1-litre ionization chamber, approximately 7000 electrons per second are generated due to the natural ambient radiation of approximately 100 nSv/h, which corresponds to a current of about 10^{-15} A. Very precise measurement technology (here: electrometers) is required to measure these very low currents reliably.

In the case of typical measurements, ionization chambers generate currents in the order of magnitude of 10^{-13} A, i.e. 0.1 picoampere. They are thus greater by two orders of magnitude than the so-called background, but are still very small. In Figure 3, the orders of magnitude of the currents are shown for various typical ranges in which they occur.

Figure 1: Photo of the secondary standard ionization chamber for the measurand "ambient dose equivalent $H^*(10)$".

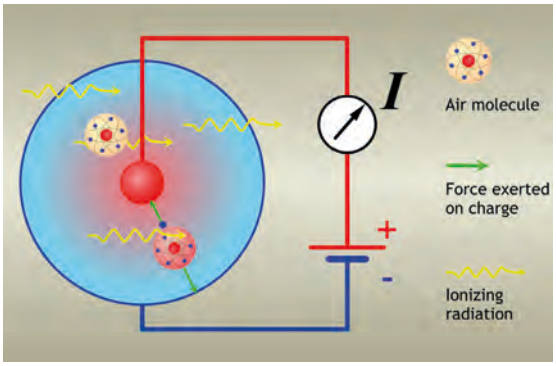

Figure 2: Measurement principle of an ionization chamber. The electrons generated by the ionizing effect of the radiation are a measure of the dose.

In *Geiger-Müller counting tubes*, gas is ionized by the radiation in the same way as in an ionization chamber. Compared to the ionization chamber, however, a much higher acceleration voltage is applied to the counting tube. This voltage causes the generated charge carriers in the counting tube to be accelerated to such an extent that many other charge carriers are generated by additional collisions with the counter gas (avalanche effect). These multiple charge carriers generate a large charge pulse and can then be detected more easily. However, the disadvantage of this measurement principle is that information on the incident radiation energy gets lost.

Proportional counting tubes, too, are operated with a higher accelerating voltage than in the case of the ionization chamber. Contrary to the Geiger-Müller counting tube, they are operated, however, with a considerably lower accelerating voltage. Thus, the number of charge carriers has increased and will be proportional to the energy of the radiation, and there will not be an indeterminate avalanche effect. The energy of the radiation can be concluded from the height of the charge pulses.

Scintillation detectors exploit the property that

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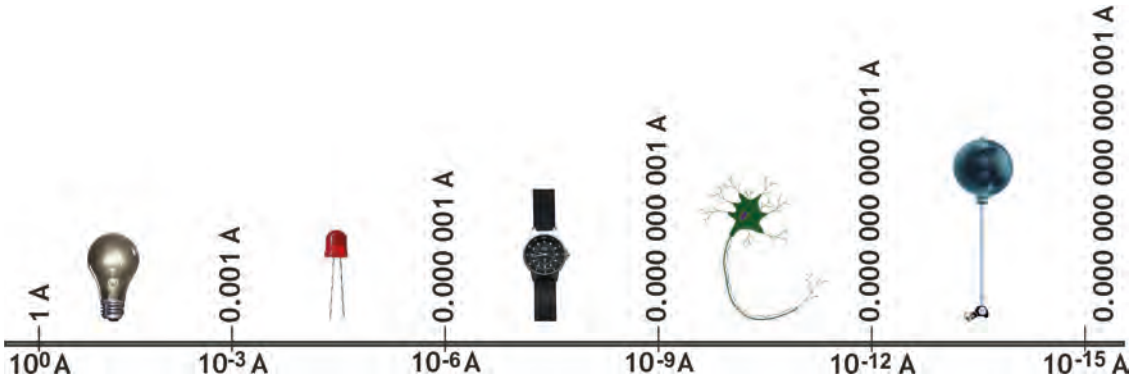

Figure 3: Orders of magnitude of different currents. The currents occurring in radiation protection metrology are approximately 1 million times smaller than the currents in a nerve cell.

substances can be directly made to glow (luminesced) by ionizing radiation. The light created in the scintillation material is measured by a highly sensitive light detector, e.g., by means of a photomultiplier.

Thermo-luminescence (TLD) or *photo-luminescence detectors* (PLD, OSL) take advantage of the fact that the ionizing radiation leads to temporary modifications in the crystal lattice which can be reversed by a subsequent energy supply, e.g., by increasing the temperature or by light irradiation. The energy which is released in this way will be emitted as flash light and can, in turn, be measured by means of a highly sensitive light detector. The overall light quantity of the light flashes is a measure of the dose.

Semiconductor detectors operate similarly to gas ionization chambers. However, as they are solids, their density and their atomic number are considerably higher, and thus a higher yield can be achieved at measurable charge carriers even with smaller detectors. The number of the generated charge carrier pairs is proportional to the energy of the incident radiation.

Films exploit the fact that the radiation causes a blackening, as in the case of incident visible light. By measuring the optical density of the processed films, the dose can be determined. In order to achieve a large measurement range, usually two different films are used: one highly sensitive film for measuring small dose values, and a less sensitive film for higher dose values.

From the detector to the dosemeter

In addition to the requirement of being able to measure – besides large signals – also very small signals, the respective detectors must also have a measurement capacity (response) which, with regard to the effects of radiation energy and of the angle of incidence, corresponds to the respective measurement dose equivalent (see the article "Measurands in Radiation Protection" in this publication). This can be achieved by means of suitable detector materials or by additional suitable filters for the adaptation of the energy dependence and of the angular dependence of the response (see Figure 4).

Dosemeters which indicate the dose that has been calculated from the detector signal directly during the measurement are called *direct-reading* or *active* dosemeters. Examples of this are, e.g., the electronic personal dosemeter of the type EPD Mk2 which is shown in Figure 5. If the readout is not realized directly during the measurement but after the measurement (and, if applicable, after a special evaluation procedure, e.g. after film processing) at another instrument, such as a computer or a readout device, they are called *passive dosemeters*; this includes film or TLD dosemeters or the DIS-1 dosemeter.

Thus, a complete *radiation protection dosemeter* consists of a radiation detector with suitable signal acquisition, the energy and angle filters in the dosemeter probe which suit the detector, as well as a function to display the measurement result. The article "Official Personal Dosimetry for Medical Staff" in this publication additionally addresses

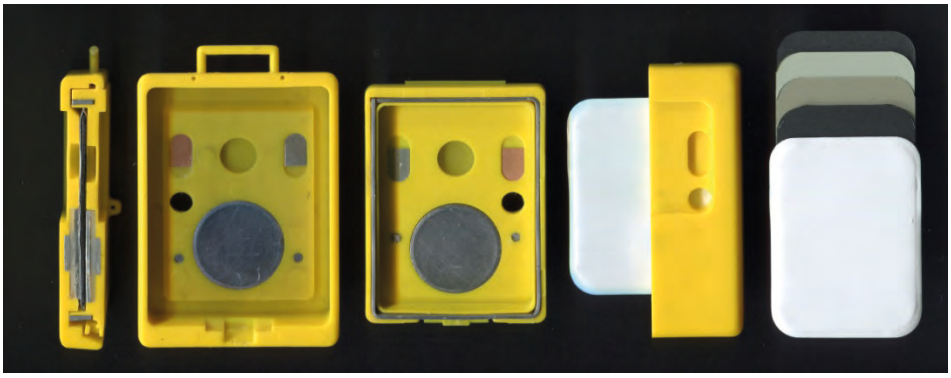

Figure 4: Gliding-shadow film dosemeter probe. From left to right: Cross section of the probe, the upper part of the probe, the lower part of the probe, half of the probe with the whole film inserted, and the open film parcel. The two energy and angle compensation filters (plastic on top, lead below) have been inserted into the yellow probe parts. The processed film is measured optically after the chemical development.

Figure 5: Area dosemeter, hand-held equipment, type 6150AD6/E with additional scintillation probe, type 6150AD-b/E (in the picture: the large device at the back: Automess Co.), and an electronic personal dosemeter, type EPD Mk2 (the small device in the front: Thermo Fisher Scientific Co.).

the question as to how the measurement trueness can be ensured by means of a type test and type approval by PTB.

The article "Measurands in Radiation Protection" in this publication addresses the fact that a distinction must be made between the measurands "area dose" and "personal dose". It follows from the diverging definitions of the measurands that two different dosemeter types must be used for the measurements: area dosemeters and personal dosemeters (Figure 5). Due to this fact, further technical requirements arise for the measuring instruments.

Personal dosemeters are worn on the trunk of the person who is to be monitored. Therefore, this instrument must be small and light. Electronic direct-reading instruments require a battery. For reasons of weight, the energy consumption of the dosemeter must be very low.

Area dosemeters can be used in two ways – on the one hand, fixed in place, for the monitoring of an area and, on the other hand, as hand-held equipment for measurements at different locations. In the form of hand-held equipment, electronic direct-reading area dosemeters can be equipped with a battery having a larger capacity, as the instrument will only be used for short-term measurements. In the form of an instrument that is fixed in place, these instruments are connected to a permanent power supply.

Measurands in Radiation Protection

Peter Ambrosi*, Oliver Hupe**

Preliminary remark

The translation of the two English terms *equivalent dose* and *dose equivalent* into German is not directly possible. In German, only one term is used – the term *Äquivalentdosis* – which is the direct word-for-word translation of *equivalent dose*. In an attempt to find, also in the German language, a reasonably logical and elegant way to deal with both terms (*equivalent dose* and *dose equivalent*), the current draft of the German standard DIN 6814-3 [1] introduces new and consistent terms and definitions for the dosimetric quantities that are used in radiation protection. The *Äquivalentdosis* is the general term for the ensemble of all dosimetric quantities in radiation protection. The physical definition of all the dosimetric quantities that are contained in the ensemble remains unchanged. Literally translated, the *Äquivalentdosis* is *equivalent dose*, and this is the term which will be used as the general term in this article. It should be noted though that the term *dose equivalent* could be used just as well. The translation of the "novel" German terms and definitions in this article back into English is, admittedly, arbitrary and should, as such, if the concept given in Figure 1 is adopted in English, be done by competent bodies.

As any misinterpretation is no longer possible, the correct terms can, in some cases, be abbreviated, e.g., *personal measurement equivalent dose* to *personal dose*.

Absorbed dose

The physical base measurand for radiation protection is the absorbed dose, D. It is defined as the ratio between the *energy transferred to a mass element* and the *mass of the mass element*. The exact definition can be found in German in standard DIN 6814-3 [1]. This standard also contains further detailed information.

The unit of absorbed dose is the joule per kilogram, with the special name *gray* (Gy), named after the English physicist Louis H. Gray (1905–1965). The following is valid: 1 Gy = 1 J/kg.

Equivalent dose

The base measurand *absorbed dose* is, however, not always suitable for all situations in radiation protection because it does not always allow us to clearly determine the risk that is associated for humans with a specific dose. The reason for this is, on the one hand, that different effects can be expected for the same absorbed dose, depending on the radiation type (whether it is alpha, beta, photon or neutron radiation). The term used in this context is "**R**elative **B**iological **E**ffectiveness" (RBE). In addition, the different organs of the body exhibit different radiosensitivities. All this must be taken into account when deciding on a dose quantity that is suitable for radiation protection.

For radiation protection purposes, the *International Commission on Radiation Protection* (ICRP) and the *International Commission on Radiation Units and Measurements* (ICRU) have implemented and specified *weighting factors* by which the absorbed dose is multiplied. These dimensionless weighting factors allow the varying biological effectiveness of the different radiation types and energies – and the different radiosensitivities of the different body organs and tissues – to be taken into account already in the dose indication. This leads to the dose term *equivalent dose*, which is used in radiation protection as the product of an absorbed dose and one or several weighting factors. The equivalent dose has the same physical unit (SI unit) as the absorbed dose, i.e. the joule per kilogram (J/kg). For a better distinction, the unit of equivalent dose was designated by the ICRU with the special unit name *sievert* (Sv), after the Swedish physicist Rolf M. Sievert (1896–1966). The following applies: 1 Sv = 1 J/kg.

EXAMPLE: If the absorbed dose of 1 mGy is multiplied by a weighting factor $w_R = 20$, the (biologically weighted) equivalent dose of 20 mSv is obtained.

Different equivalent dose quantities

Radiation exposure may affect the whole body, or only single organs. Furthermore, the irradia-

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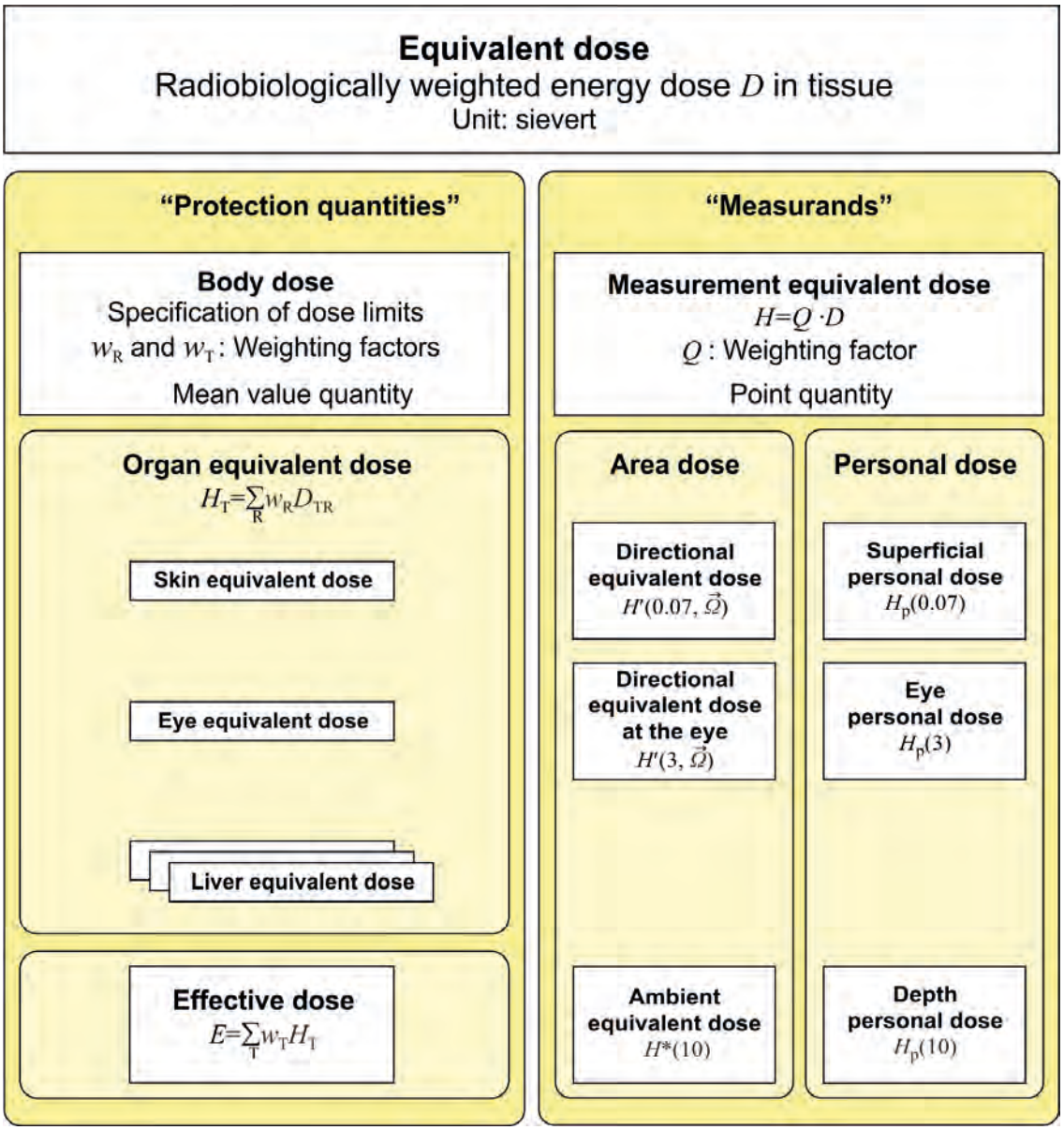

Figure 1: Concept of the dose quantities in radiation protection, in accordance with the German standard DIN 6814-3 [1], translated literally from German, see the "Preliminary remark" at the beginning of this article.

tion may be applied from the outside (e.g., during "X-raying"), or from the inside (e.g., during "scintigraphy"). As these different ways of exposure require suitable dose quantities, radiation protection encompasses a number of different quantities. For laying down dose limits for laws or ordinances, the organ equivalent dose H_T is used – as it relates directly to the human body. For radiation protection measurements, the equivalent dose H is the central term.

The relationship outlined above is shown – in English – in Figure 1 and (for comparison purposes) in Figure 2 also in German.

Stochastic and deterministic radiation effects

One of the central tasks of radiation protection is to limit the radiation exposure of the general population, of patients, and of persons who are occupationally exposed to radiation. The intention of this is to rule out the occurrence of radiation detriment – or to keep such a detriment, at least, to a justifiably low value. A distinction is made between the stochastic and the deterministic detriment. In the case of *stochastic radiation effects*, e.g. cancer, the probability of a radiation detriment occurring depends on the magnitude of the exposure, i.e. on the dose. After the detriment has occurred, the severity of this radiation detriment does not depend, however, on the dose that has been received before. Due to the fact that the investigation of the radiation risks occurring through an exposure to low doses has not been terminated yet, it is usually assumed (in accordance with the precautionary principle) that there is a linear relation between the probability of a detriment occurring and the dose having been received before, and that no threshold value can be given below which the risk of radiation effects could be

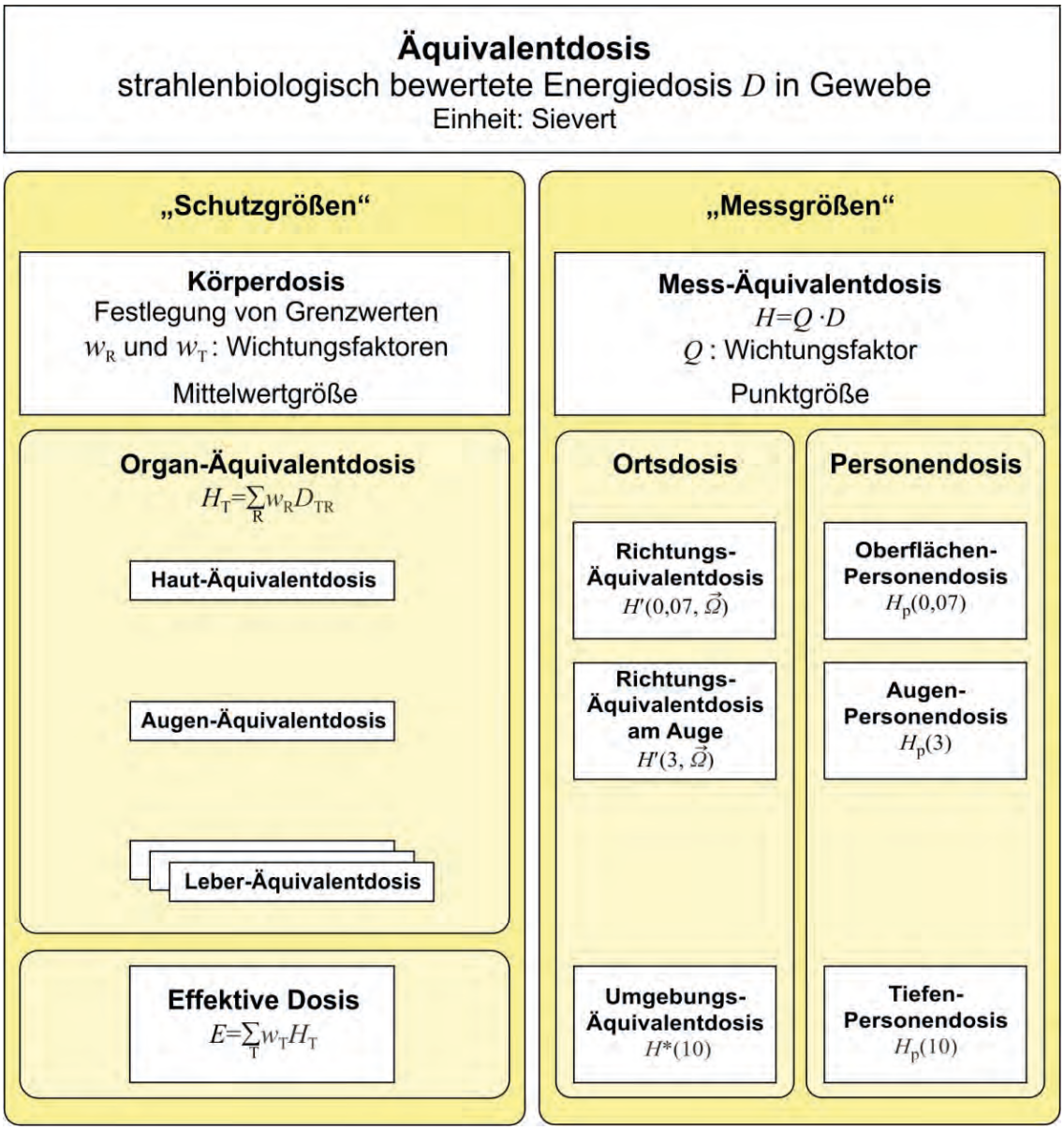

Figure 2: Concept of the dose quantities in radiation protection, shown – for comparison purposes – also in German, in accordance with the German standard DIN 6814-3 [1].

ruled out. This is also known as the “Linear No Threshold (LNT) Model”, ICRP 103 [2]). *Deterministic radiation effects* are effects where the radiation detriment (e.g. skin reddening) occurs with certainty, but only after a certain dose threshold has been exceeded. Thereby, the severity of the radiation detriment depends mainly on the dose having been received before.

Body dose and measurement equivalent dose

According to today’s concept of radiation protection, the radiation exposure of radiation-sensitive organs of the body is applied to assess the stochastic risks. Thereby, it is usually sufficient to use the mean dose in organs. As the individual organs have different radiosensitivities, it has proved convenient to represent the magnitude of a total exposure as the weighted sum over the organ equivalent doses. Thereby, organs with a high radiosensitivity are assigned a numerically higher weighting factor than organs with a low radiosensitivity. The tissue weighting factors are usually denoted by the symbol w_T (with the index T standing for the word “tissue”). The *effective dose* is formed as the sum of the organ equivalent doses, using the tissue weighting factors recommended by the ICRP. Today, the effective dose is regarded as the measure for the magnitude of a radiation exposure for stochastic radiation effects. As a consequence, the effective dose is used when it comes to laying down the dose limits in radiation protection legislation. All dose terms which are required for that purpose are summarized under the generic term *body dose* (see Figures 1 and 2).

As already mentioned above, the biological effect of an exposure depends not only on the absorbed dose, but also on the type of radiation (alpha, beta, photon or neutron radiation) and on the energy of

the radiation. For the determination of body doses, this fact is taken into account by the application of the radiation weighting factor w_R (with the index R standing for the word "radiation"). This means that all the dose quantities which are summarized under the generic term *body dose* belong to the category of the radiobiologically weighted dose quantities and represent, thus, an equivalent dose. They are shown in the left part of Figures 1 and 2.

For practical applications, this simple concept has the decisive disadvantage that the dose values of the organs in the human body cannot be determined metrologically. To solve this problem, a second group of dose quantities (summarized under the generic term *measurement equivalent dose* – on the right of Figures 1 and 2) has been created. The measurement equivalent dose also contains radiobiological weighting. Here, this is, however, realized by means of the quality factor Q. The difference between weighting by means of the quality factor Q and weighting by means of the radiation weighting factor w_R will be briefly explained below. The measurement equivalent dose quantities have primarily been defined under protection aspects, i.e. to guarantee a – usually – conservative estimation of the body dose to be imaged, without allowing inadmissibly large overestimations of the body dose that has to be imaged.

For the treatment of deterministic radiation detriment, the considerations above can be used correspondingly for body and measurement equivalent doses. In the case of deterministic radiation effects, the dose usually does not occur as the sum of the weighted organ equivalent doses, but in one single organ, in which detriment due to the exposure conditions is to be suspected. Very frequently, the skin is affected. It is, however, also valid here that the actual magnitude of the radiation exposure which is to be determined by means of the body dose cannot be measured directly. Therefore, again, the measurement is carried out with a suitable quantity taken from the group of the measurement equivalent dose quantities.

Area dose and personal dose

Body doses can be determined approximately: either by carrying out measurements directly on the person who is to be monitored, or – independently of the presence of a person – at a specific place in the room. Accordingly, the doses are called *personal dose* or *area dose*.

The *personal* (*equivalent*) *dose* $H_p(d)$ [3] is defined as the measurement equivalent dose in the body tissue at a depth d, measured at a "place of the body surface which is representative of the exposure". If the whole body is exposed to penetrating radiation, *the depth personal dose* $H_p(10)$, with the depth d = 10 mm, is selected to estimate the effective dose, as this depth estimates the tissue depth of most organs conservatively. To estimate the skin dose equivalent if only partial areas have been exposed (frequently only the hands), the *superficial personal dose* $H_p(0.07)$ [3], with the depth d = 0.07 mm, and, for the estimation of the eye equivalent dose, the *eye personal dose* $H_p(3)$ [3], with the depth d = 3 mm, are measured.

The personal dosemeter has to measure the dose in the person. Therefore, it must always be worn on the body of the person when the measurement is carried out. These measurements serve to determine the dose a person has received during his/her stay in the radiation field. When the personal dosemeter is calibrated, care must, therefore, be taken that the dosemeter is always irradiated on a phantom, which serves as a substitute for a person.

Today, *area dosimetry* is based on the *ICRU sphere* [3]. This sphere has a diameter of 30 cm and consists of a very precisely specified material (density: 1 g/cm^3) which is equivalent to human tissue. As this material is, above all, used for theoretical considerations and fundamental computed simulations, it is of no particular importance that it has so far not been realized physically.

When the ICRU sphere is brought into a radiation field, this field is modified as if a real person were present in this particular place.

The two area dose quantities *ambient equivalent dose* and *directional equivalent dose* have been developed on the basis of the ICRU sphere. The *ambient equivalent dose* $H^*(10)$ [3] serves to estimate the effective dose, the *directional equivalent dose* $H'(0.07)$ [3] serves to estimate the skin equivalent dose, and the *directional equivalent dose at the eye* $H'(3)$ [3] serves to estimate the eye equivalent dose. In many countries, among them Germany and the other EU countries, mainly the two area dose measurands $H^*(10)$ and $H'(0.07)$ are used in practical radiation protection.

The area dosemeter is used to measure the dose which a person who is present at the place of measurement would receive. The area dosemeter is designed in such a way that it does not need to be positioned on the body surface of a person or on a phantom (ICRU sphere) to fulfil this task. Also when an area dosemeter is calibrated, care must be taken that it is irradiated without an additional phantom.

The difference between w_R and Q

The weighting factors w_R and Q use the influences of the radiation type and of the radiation energy in a different way. The w_R factors refer to the radiation type *at the radiation source* and are derived from experimentally determined values

of the relative biological effectiveness for the cancer-producing effect of the radiation observed. The quality factor Q relates to the radiation type existing at the *place of measurement*. With the aid of the *linear energy transfer* (LET) of the charged particles of the radiation which are responsible for the energy deposition, the value of the quality factor Q can be determined in such a way that the biological effectiveness is modelled. The quality factor Q is, however, defined purely physically. In spite of that, it reflects the biological effect of the radiation.

Literature

[1] DIN "Begriffe in der radiologischen Technik – Teil 3: Dosisgrößen und Dosiseinheiten", DIN 6814-3, draft of March 2013

[2] ICRP, "The 2007 Recommendations of the International Commission on Radiological Protection", ICRP Publication 103, Ann. ICRP 37 (2–4), 2007

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Official Personal Dosimetry for Medical Staff

Oliver Hupe*

Overview

Official personal dosimetry ensures that the dose limits laid down in the X-ray Ordinance and in the Radiation Protection Ordinance are being complied with. Pursuant to Art. 35, Para. 1 of the X-ray Ordinance, the following applies: "The body dose on persons who stay in the control area for reasons other than their own medical or dental examination has to be determined immediately ..." Furthermore, pursuant to Para. 4, the following also applies: "The body dose is to be determined by measuring the personal dose. The competent authority designates bodies for the measurements according to Clause 1 ..." Official individual dose monitoring means that the dosemeters are handed out and – subsequently – analysed by an individual monitoring service which has previously been designated by the competent authority.

In order to ensure measurement trueness, only verified dosemeters may be used for those measurements, which serve health protection. In Germany, approx. 350,000 persons are occupationally exposed to radiation; approx. 70 % of them work in the medical sector.

Observance of the dose limits ensures that the radiation exposure experienced by a person does not lead to unacceptable negative health effects due to radiation. For this reason, the dose values for persons who are occupationally exposed to ionizing radiation are measured continuously and determined at regular intervals (usually monthly) by means of official dosemeters. In Germany, to date only passive dosemeters – i.e. dosemeters which do not display the dose value measured directly on the dosemeter – have been approved as official dosemeters. Depending on the type of radiation exposure, either whole-body dosemeters or additional partial-body dosemeters are issued.

Official dosemeters may only be issued and analyzed by individual monitoring services. The dose values which have been officially determined by the individual monitoring services are saved in the national dose register. The dose register provides, besides the safeguarding of the data, also the possibility to carry out statistic surveys on radiation exposure in different areas. These data can then also be used to improve radiation protection in particularly exposed areas. An example of this is the exposure radiation of the medical staff where radionuclides are used in nuclear medicine.

If it can be expected that the annual dose limit will be exceeded if the activity remains the same, then the person concerned is relocated in due time to another working environment with less or no radiation. In this way, the use of dosemeters indirectly ensures that exceeding the dose limit is prevented, even though the dosemeter itself does not, of course, offer protection from radiation (contrary to what one might think when the term "radiation protection dosemeter" is used).

Quality assurance by means of type testing and verification

Verification has already been mentioned as a precondition for measurement trueness. To pass verification, a dosemeter needs a type test and type approval issued by the Physikalisch-Technische Bundesanstalt (PTB). PTB puts the dosemeter to the test. The mandatory requirements to pass the approval test are laid down by the Verification Ordinance and by the PTB requirements for radiation protection dosemeters. The national PTB requirements are elaborated according to the state of the art in science and technology and to the international testing standards (IEC); they are correspondingly adjusted from time to time. If the type approval – which is only valid at the national level – is in agreement with the international standards, it will also be recognized internationally and will be considered as a proof of quality of the dosemeter. This is ensured through PTB's active participation in the international standardization bodies.

The type test is carried out only once, as an exemplary type examination. The overall measurement trueness and measurement reliability that

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are thereby determined are certified by means of the authorization for national verification. The manufacturer must then produce all further specimens of this dosemeter type identically to the type tested by PTB; if any modification is made, it has to be approved by PTB, too. Verification is then the regular individual check of the dosemeter with regard to solely one or a few of the verification items determined upon approval. The thorough type test carried out by PTB, combined with regular verification by the local verification bodies, provides a high level of measurement trueness.

The "International Commission on Radiological Protection" (ICRP) has laid down the minimum requirement according to which the measurement uncertainty of the effective dose must be smaller than ± 50 % [1]. This value, however, applies taking all influence quantities – such as, e.g., temperature, time, and especially energy and angle of incidence of the radiation – into account; it can therefore be reached only by good-quality devices. The proof of the quality of a measuring instrument is provided by the type approval issued by PTB. An updated list of all type-approved area dosemeters and personal dosemeters can be consulted on PTB's website.

Another challenge in official dosimetry consists in correctly taking the contribution of natural environmental radiation into account. Here too, influence factors such as, e.g., the storage of the dosemeters while they are not being used (for example, in a desk drawer or in a repository hanging on a wooden or concrete wall), have to be taken into consideration. A concrete wall may considerably increase the natural environmental radiation. The dose due to natural environmental radiation amounts to approx. 2 µSv per day, i.e. about 60 µSv per month; depending on the local conditions, it can, however, vary by a factor of 2 or even more. Hereby, the additional dose which can be detected reliably by official personal dosimetry amounts to 100 µSv per month only. This small value is necessary to be able to comply with the minimum value of 1 mSv per year for the effective dose of individuals in the population.

For the quality assurance of official dosimetry by the individual monitoring services, PTB carries out annual comparison measurements, since it is not possible to verify each passive dosemeter singly (for instance, a film can only be used once and would no longer be utilizable after verification). For this purpose, the individual monitoring services send 15 dosemeters of each type of dosemeter issued every month or every three months to PTB. At a time determined by PTB but not known to the individual monitoring services, these dosemeters are irradiated with a dose which is not known by the individual monitoring services. These irradiated dosemeters are submitted to the respective verification authorities. The latter take these – on the occasion of an unannounced visit – to the individual monitoring services to have them analysed within the scope of a routine examination in their presence. The dose values determined in this way are sent to PTB, which then decides whether the dosemeters comply with the requirements [3].

Individual monitoring in practice

The official passive personal dosemeter most commonly used in Germany is the gliding-shadow film dosemeter (as shown in Fig. 1) which was developed by PTB and the individual monitoring service at the *Materialprüfungsamt Nordrhein-Westfalen*. Here, the dose is determined from the optical density (blackening) of the film (see the article "Measuring Instruments and Challenges in Radiation Protection Metrology" in this publication).

The ICRP makes proposals for the dose limits – currently in ICRP Recommendation 103 [2]. These recommendations are then usually transposed into European legislation. At present, an important topic of discussion is the introduction of a new dose limit for the eye lens, as indicated by the ICRP in a recommendation dated October 2011. Examples of dose limits are listed in Table 1.

The unborn child of a pregnant woman is categorized as a person of the population in general, even if the pregnant woman herself is occupationally exposed to radiation. Hence, the annual dose limit of 1 mSv applies to the unborn child, too. In order to ensure compliance with this value, it is no longer sufficient to measure the dose monthly, but rather a weekly dose determination is then necessary. This cannot be reliably ensured with passive dosemeters such as, e.g., a film dosemeter. There-

Figure 1: A personal dosemeter, here the gliding-shadow film dosemeter, measures correctly only when the person using it wears it on his/her trunk. For calibration, the dosemeter must therefore be placed on a phantom.

Body dose	Organ	Annual dose limit for persons occupationally exposed to radiation	Annual dose limit for the population in general
Effective dose	Whole body	20 mSv	1 mSv
Organ dose	Eye lens	150 mSv (soon 20 mSv?)	15 mSv
	Hands, forearms, feet, ankles	500 mSv	50 mSv
Local skin dose		500 mSv	50 mSv

Table 1: Examples of legally determined annual dose limits, based on the mandatory European Directive EURATOM 96/29

fore, it is necessary to wear an additional, verified electronic or direct-reading personal dosemeter. For more information on these dosemeters, please read the article "Electronic Dosemeters for Pulsed Radiation" in this publication.

What is essential in individual dose monitoring is the selection of the appropriate dosemeter and of the suitable place to wear it. When selecting the dosemeter, attention must be paid to choosing a suitable energy region. In the medical field, the mean photon energy can amount to less than 20 keV, e.g. in mammography. Not all of the approved electronic personal dosemeters are able to comply with the PTB type-approval requirements at such a low energy and are therefore only approved for use in radiation fields with higher energy. As far as the place for wearing the dosemeter is concerned, it is the responsibility of the person in charge of radiation protection and of the monitored person to select a place which is "representative for the exposure of the body surface". Another aspect which is just as important is whether the personal dose equivalent $H_p(10)$ (for the estimation of the effective dose) or the personal dose equivalent $H_p(0.07)$ (for the estimation of the skin dose) also have to be measured. Typical ways of wearing a dosemeter are shown in Fig. 2.

Figure 2: Typical ways of wearing dosemeters: gliding-shadow dosemeter (whole-body dosemeter, measurand $H_p(10)$) worn on the trunk, finger-ring dosemeter (partial-body dosemeter, measurand $H_p(0.07)$) worn on the finger which is closest to the radiation source, and an additional direct-reading electronic personal dosemeter (whole-body dosemeter, measurand $H_p(10)$).

Literature

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Dose for Assisting Persons in Human Medicine, Dentistry and Veterinary Medicine

Oliver Hupe*

Overview

For persons who work in – or must be present in – controlled areas, it is necessary to determine the body dose. Besides persons who are occupationally exposed to radiation, also persons who assist in human medicine and dentistry as well as in veterinary medicine by calming down and holding the patients or animals during an examination belong to this group. For this reason, PTB measured, within the scope of a research project funded by the *Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety* (BMUB) and the *Federal Office for Radiation Protection* (BfS) [1], the dose received by assisting persons during X-ray examinations. In the appurtenant final report [1], not only the text extracts quoted here, but also further details can be consulted.

For the measurements, attention must be paid to the fact that the radiation used in X-ray diagnostics is pulsed, in order to avoid motion unsharpness. For that reason, the suitability of the dosemeters used to measure pulsed X-rays had to be checked first of all. For more information on the general problem, please read the article "Electronic Dosemeters for Pulsed Radiation" in this publication. Since the assisting persons are in motion and have to take different positions to hold the patients (depending on the situation), it is not possible to carry out repeat measurements, even if the same recording scenario is used. Furthermore, any superfluous exposure to radiation must be avoided, so that also for that reason, repeated measurements would not be possible. Such a summing up of the low dose values to improve the measurement accuracy would, however, be the pre-condition to be able to use passive measuring instruments such as, e.g., TLD dosemeters which have no problem measuring pulsed radiation. It is therefore necessary to use electronic, direct-reading dosemeters.

The measurements which had to be carried out for this project were complex – not only due to the very low dose values which were difficult to measure, but also because the "in-situ" measurements were not supposed to disturb the routine sequence of the X-ray examinations – i.e. the assisting persons had to be equipped with measuring instruments quickly. Detailed measurements with more precise ionization chambers could, thus, only be performed in simulated laboratory measurements. The results obtained, however, confirmed the dose values which had been determined "in situ" by means of the electronic dosemeters.

Demanding measuring technology

Due to the above-mentioned requirements, for the measurements under laboratory conditions, two different secondary standard ionization chambers were used, for the ambient dose equivalent $H^*(10)$ and for the personal dose equivalent $H_p(10)$, whereas for the "in-situ" measurements, the electronic personal dosemeters of the type EPD Mk2 were used [2][3]. Both ionization chambers are characterized by the low energy-dependence of their response. Furthermore, their responses remain nearly constant over a large dose- and dose-rate range.

For the measurements with the ionization chambers, a special electronic unit was developed at PTB by means of which the very low amount of charge occurring during these short irradiation times can be separated from the charge generated by leakage currents or disturbances. The core piece of the electronic unit is an electrometer for charge measurement which was developed at PTB. Furthermore, the electronic unit includes a high-voltage module for the chamber voltage, sensors to measure the temperature, the humidity and the pressure, as well as a notebook equipped with measurement and analysis software which was written at PTB. For the measurements at the veterinary clinic, it was necessary to design this

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metrological equipment in such a way that it could be transported.

The electronic personal dosemeter used (EPD Mk2) has a type approval and, thus, complies with the corresponding requirements placed on the type by PTB. The photon energy range tested (from 16 keV) includes the range occurring in the measurements so that it is also suitable for the measurement of the low-energy scattered radiation.

For the assisting persons, the dose to be measured lies in the range from 0.01 µSv to 30 µSv (depending on the X-ray examinations). The dose values displayed by the electronic personal dosemeter used are, however, indicated in gradations of 1 µSv, which are too large for this purpose. With the optional infrared interface of the dosemeter it is, however, possible to read out the dose values in steps of 0.01 µSv instead. The approved dose range of the EPD Mk2 extends from 10 µSv to 10 Sv. A preliminary investigation has shown that when using the optional infrared interface, also the dose indication below 10 µSv complies with the PTB requirements.

Contrary to the rules of radiation protection, the EPD Mk2 dosemeters were placed on top of the protective clothing. This was necessary because the dose values occurring thereby were so low that measurement underneath the protective clothing would not have been possible. Therefore, the dose values determined apply to assisting persons who, by mistake, are not wearing protective clothing. The protective clothing reduces the dose by a factor between 10 and 100. In some "in-situ" measurements, only few assisting persons were present, so that the EPD Mk2 dosemeters had to be set up on stands without backscattering bodies. A preliminary investigation had shown that for this type of dosemeter and for the corresponding radiation fields, the influence on the result of the person wearing it and of the phantom, respectively, is smaller than 2 % and therefore negligible. The measurement results are thus representative.

In addition, to assess the risks for assisting persons, attention must be paid to the fact that wearing protective clothing can reduce the occurring dose values by a factor of up to 100 (depending on the type of protective clothing and on the high-voltage set).

Dentistry

Representative examination scenarios in dentistry were determined both by interviewing experts and by means of observations and talks in clinics for oral and maxillofacial surgery (OMS) of the Hannover Medical School (*Medizinische Hochschule Hannover* – MHH).

Dental X-ray examinations can be classified into 4 types: (1) panoramic radiograph of the dentition, (2) intraoral radiograph of individual teeth, (3) extraoral X-ray lateral radiograph, and (4) digital volume tomography (DVT) – which is rather infrequent. The tube high-voltages adjusted are in the range between 40 kV and 110 kV.

Figure 1: Since assisting persons are needed only very rarely in dentistry, the electronic dosemeters (EDP Mk2) were placed, for the measurements, where the auxiliary person would usually be sitting. Both the patient and the chair representing the assisting person are wearing protective clothing.

The presence of assisting persons during radiological examinations may be necessary in the case of infants, physically impaired persons or persons suffering from dementia. If possible, the X-ray room should be left by the assisting persons for the short moment during which the actual radiograph is taken.

Figure 1 shows a typical situation of a panoramic radiograph. The patient is seated on a chair while the X-ray device moves around her. Normally, the assisting person would sit next to the patient on a chair, outside the pivoting range of the X-ray facility. Since assisting persons are, however, needed only very rarely in dentistry, for these measurements the electronic dosemeters (EDP Mk2) were placed where the assisting person would usually be sitting.

In dentistry, the dose values measured on top of the protective clothing (for the assisting persons) lie, depending on the type of examination, in the range from 0.1 µSv to 4 µSv; this is comparable to the daily dose due to natural environmental radiation (approx. 2 µSv).

Veterinary medicine

In veterinary medicine for large animals (horses), measurements were carried out both in veterinary clinics and during "in-situ" X-ray examinations (in the stables). In Fig. 2, for comparison purposes, the same type of examination is shown: once in the stables ("in situ") (on the left) and once at the veterinary clinic (on the right). In both situations,

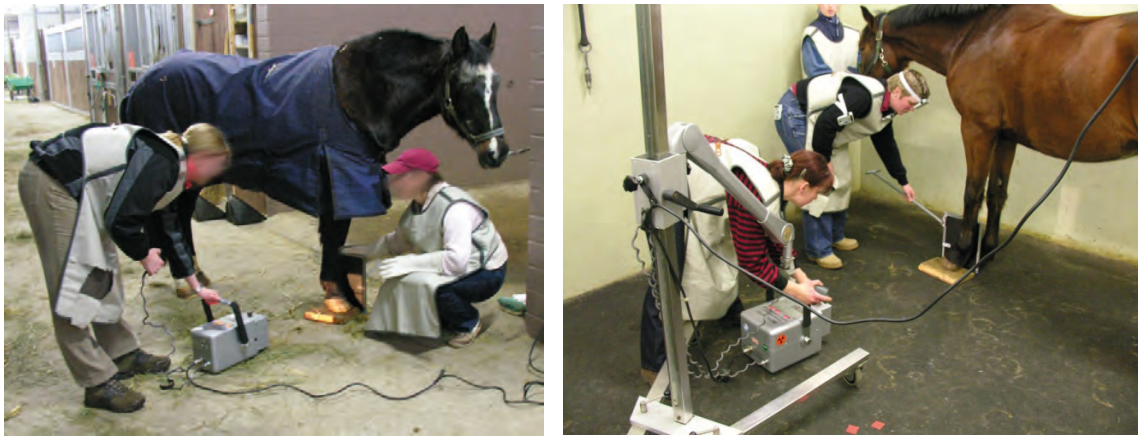

Figure 2: Examination of a horse leg; picture on the left: "in-situ" situation; picture on the right: clinical situation.

the dose values measured for the assisting person are comparable.

To determine in detail the dose and the angular distribution of the scattered radiation occurring during the examination of small animals, the scattering properties of small animals were investigated at the X-ray facility of PTB. To this end, two special animal phantoms were made of PMMA ("plexiglass"): a dog phantom and a cat phantom (see Fig. 3). Comparison measurements carried out on dead animals at a clinical diagnostic X-ray facility of the University of Veterinary Medicine Hannover have shown that these laboratory results can be transferred to the dose values for the assisting persons.

For the measurements performed with the phantoms, the X-ray fields used in veterinary medicine were reproduced at one of PTB's X-ray facilities. The tube high-voltages for these measurements were in the range between 50 kV and 90 kV. The dose was measured in the scattering radiation fields both with the EPD Mk2 dosemeters and with the $H^*(10)$ secondary standard chamber.

In the field of veterinary medicine, the highest dose values of approx. 30 µSv occur when small animals (dogs) have to be held, measured on top of the protective clothing since the distance between the assisting person and the animal – and thus the scattering radiation source – is the smallest here and the radiation field is set at its maximum. In other examinations, the dose values are considerably lower.

Human medicine

Assisting persons in human medicine are required mainly for orthopaedic examinations. During dose-intensive examination processes such as, e.g., CT and angiography, no assisting persons are present.

For measurements in human medicine, the focus lay on not disturbing the routine sequence. For that reason, several dosemeters were placed on stands in different places. This allowed several measured values to be obtained simultaneously during a single X-ray examination (see Fig. 4). As already mentioned above, the measurement results obtained with the EPD Mk2 dosemeter are representative even without using a phantom.

The dose values determined on top of the protective clothing for assisting persons in the medical sector are on the order of the natural environmental radiation for approx. 12 hours up to approx. 300 hours (12 days). Hereby, the daily dose of natural environmental radiation was assumed to be approx. 2 µSv.

Figure 3: Cat phantom made of PMMA, manufactured for the detailed investigation of the scattering properties in the laboratory.

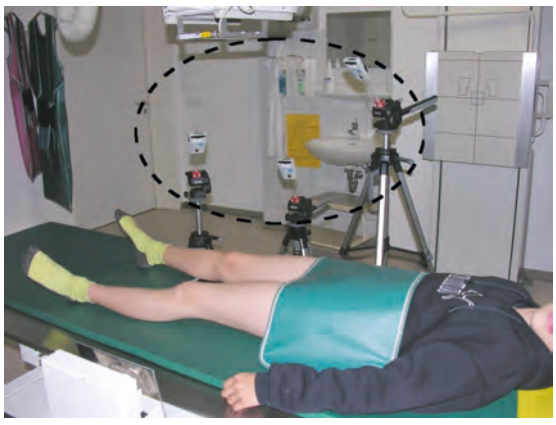

Figure 4: Measurements with electronic personal dosemeters placed on stands in places where assisting persons might be standing.

These low dose values apply only if the assisting person stays exclusively in the scattering radiation field. Possible accidental situations (i.e. the assisting person gets into the direct beam) were not considered within the scope of the investigations. In order to protect persons in the event of such accidents, the prescribed radiation protection measures (e.g. wearing lead aprons) must be complied with. Possible partial-body exposures – as might occur due to the unpermitted holding of patients in the direct beam area – are also considered as accidental situations. In the event of an accident, higher dose values would have to be expected for the assisting person.

To ensure the traceability of all determined dose values to primary standards, the measuring instruments used were calibrated at PTB in the typical diagnostic radiation fields.

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Partial-body Dosimetry for Photon and for Beta Radiation

Rolf Behrens*

Introduction

There are workplaces where radiation hits the body rather non-uniformly, i.e. the radiation field is inhomogeneous. This case occurs, on the one hand, when the staff work relatively close to the point of origin of the radiation and, on the other hand, if the radiation field is limited by apertures. It may, for example, happen that the hands – but not the trunk – are affected by radiation. In these cases, the radiation will not be recorded by the whole-body dosemeter. It is thus necessary to wear separate dosemeters on those parts of the body that are particularly exposed to the radiation, and also on parts of the body which are particularly sensitive.

Partial-body dosemeters are often used as *finger-ring dosemeters* (see Figure 1) – in particular, if mainly the hands are exposed to a (limited) radiation field. Finger-ring dosemeters serve to monitor the value for the local skin dose equivalent, its limiting value is 500 mSv per year. If this value is complied with, it can be assumed that the radiation to the skin does not lead to deterministic damage such as, for example, redness or blistering.

Recently, it has been found that the eye lens is more sensitive to radiation than it had been assumed in the past. If the radiation dose is too high, this may cause a cataract. It is, therefore, to be expected that a proposal made by the International Commission on Radiological Protection (ICRP) will be implemented also in Germany and that the presently valid dose limit of 150 mSv per year will be reduced to 20 mSv. In this case, protection by means of shielding – but also the measurement of the lens dose with the aid of *eye dosemeters* – will, in future, become ever more important (see Figure 2).

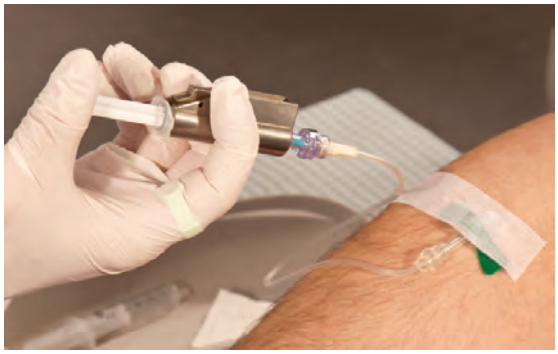

Figure 1: Nuclear-medical examination. The white finger-ring dosemeter is worn on the index finger, with the detector turned towards the syringe containing a radioactive pharmaceutical.

Figure 2: Angiography. The personal dosemeter for the eye is worn on the left side of the head in the direction of the X-ray tube.

Typical body locations of partial-body dosemeters in medicine

For some operations, X-rays are used (interventional radiology) to exactly determine the position of medical objects in the body (for example, endoscopes or catheters), e.g. in angiography (for the representation of vessels – see Figure 2) or in embolisation (closing of blood vessels, e.g. to stop the blood supply of a tumour). Here, all members of the surgical team are exposed to the scattered radiation emitted by the patient, in spite of shielding. Furthermore, the operator may reach into the direct X-ray with his hands and arms. It may thus be necessary to wear both a finger-ring dosemeter and an eye dosemeter.

In nuclear medicine, radioactive substances are inserted into the body of the patient, for example in order to use the radiation emitting from the body for imaging (this is the case, e.g., in positron-emission tomography – abbreviated to: PET – in order to represent the thyroid) or for therapeutic purposes such as, for example, in the fight against tumours, or in radiosynoviorthesis – abbreviated to: RSO (treatment of chronic arthritis). The radioactive solutions are administered by means of (shielded) syringes. In this way, especially the fingers may be exposed (see Figure 1). Here, finger-ring dosemeters are of particular importance.

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Technical details of partial-body dosemeters

In partial-body dosimetry, thermoluminescence detectors (TLDs: small crystals which light up after exposure when heated) are frequently used as these are available in relatively small dimensions (e.g. chips of 4 to 5 mm in diameter and approx. 1 mm in thickness).They are introduced into a plastic holder. The thickness of this holder is optimized in such a way that the particular depth that is representative for the organ to be monitored is reached in the material. For the eye lens, this thickness amounts to 3 mm, in accordance with the measurand "personal dose equivalent" (at a tissue depth of 3 mm), $H_p(3)$. For the skin layer which is sensitive to radiation (the epidermis), it amounts to approx. 70 µm, in accordance with the personal dose equivalent (at a tissue depth of 0.07 mm), $H_p(0.07)$. To realize the low measurement depth of 0.07 mm, in the case of finger-ring dosemeters, very thin front covers are, on the one hand, used for the TLDs (e.g. 20 µm) and, on the other hand, very sensitive detectors which exhibit a very thin active detection layer only (also in the order of a few 10 µm), so that a total thickness of approx. 70 µm is reached.

How partial-body dosemeters should be worn

As *eye dosemeters* are to estimate the dose to the eye lens, they must be worn close to the eyes, usually at the front side of the head. Only in those cases where the radiation clearly comes from a preferred angular section, and where the person wearing the dosemeter does not significantly turn around in the radiation field, should the dosemeter be directed towards the radiation source. It should, however, maximally be worn at the side of the temple, and not at the back of the head. The latter would lead to clearly too high measurement values compared to the dose to the eye lens, as the eyes would be shielded by the head, but the dosemeter would not.

Finger-ring dosemeters are to estimate the dose to the skin. Here, it is particularly important to align the dosemeters in the direction of the radiation source. Especially when radioactive substances are handled, the dosemeters must be worn on the inner side of the finger (see Figure 1). If, in these cases, the dosemeter was worn on the outer side of the finger, clearly too low measurement values would be obtained compared to the skin dose on the inner side of the finger, in particular in the case of weakly penetrating beta radiation (which is applied, e.g., in nuclear medicine) which would be shielded almost completely by the finger and, thus, would not reach the dosemeter.

In general, the following always applies: If shielding is used – e.g. a lead apron, protective goggles or gloves – the dosemeters must be worn under the shielding because the organs to be protected are also located there. If this is not possible for practical reasons (for example, in the case of protective goggles), a material layer which is equivalent to the shielding used must alternatively be positioned in front of the dosemeter to mimic the absorption effect.

Different dosemeter types in use

Like the official *whole-body* dosemeters, also the official *partial-body* dosemeters are issued and assessed by the respective dosimetry services which are in charge of this in Germany according to the laws of the respective federal states, and their quality is annually ensured by PTB by means of comparison measurements (see the article "Official Personal Dosimetry for Medical Staff" in this publication). In Germany, the number of partial-body dosemeters is clearly smaller than that of whole-body dosemeters (which amounts to 350,000 per month): Approx. 20,000 finger-ring dosemeters and, up to now, only approx. 150 eye dosemeters – the latter, however, with increasing tendency.

Up to now, eye dosemeters have measured the measurand $H_p(0.07)$ – not $H_p(3)$. At workplaces with – exclusively – photon radiation, e.g. workplaces in interventional radiology, this is acceptable as the measurement values of an $H_p(0.07)$ or an $H_p(3)$ dosemeter differ from one another only slightly if they are worn close to the eye. At workplaces with beta radiation, e.g. in nuclear medicine, it is, however, indispensable to use eye dosemeters for the measurand $H_p(3)$, because $H_p(0.07)$ dosemeters indicate, in certain beta radiation fields, a dose which is too high by a factor of 100 and more. The reason for this is that – in the case of some beta radiation sources – the range of the beta radiation may suffice to reach the detector at a depth of 0.07 mm, but not the eye lens at a depth of 3 mm. For the above-mentioned beta radiation sources, an actual lens dose in one month of, for example, 2 mSv could, thereby, generate a dosemeter indication of 200 mSv: This leads, on the one hand, to an unfounded worry on the part of the respective person and, on the other hand, to a limitation of his/her previous activity, although the limiting value for the eye lens has by far been undercut. In the case of beta radiation it is, however, mostly possible to wear sufficient eye protection, e.g. slightly thicker plastic goggles (of a few millimetres) for complete shielding against beta radiation. As always in radiation protection, we are left with the conclusion: Protective measures are the first method of choice. Optimizing dose measurement is just the second one.

Electronic Dosemeters for Pulsed Radiation

Oliver Hupe*, Hayo Zutz, Peter Ambrosi*****

Introduction

In addition to the official personal dosemeters, direct-reading electronic dosemeters with an alarm function which are acceptable for verification are used to an ever increasing extent in radiation protection monitoring. The fields of application of the dosemeters depend on the workplaces. Most of the approximately 350,000 persons who are occupationally exposed to radiation at their workplaces in Germany work in sectors where X-rays are used. In the past few years, there has been a change in medicine, industry and research – from continuous X-radiation to pulsed X-radiation.

When carrying out measurements in pulsed radiation fields as have already been used for a long time in medicine, PTB found out, in 2007, that the measurements of electronic dosemeters are reliable only to a limited extent. This is due to the method of measurement applied, which is usually of the "counting" type. [1]. Modern electronic dosemeters are mostly equipped with one or several detectors with complex measuring electronics. Consequently, a dosemeter does not only count single events by the interaction of the photons with the detector. The measuring electronics should rather also compensate for known deficits such as, for example, the dependence of the detector on the energy or the dead time. The dead time is the time in which a dosemeter – after a counted event – can no longer detect further events. The dead time is responsible for the fact that very short X-ray pulses with a high dose rate can hardly be measured. Thereby, it does not matter whether the dead time of the dosemeter is caused by the detector, by the electronic system or by both.

In 2008, the problems related with electronic dosemeters in pulsed radiation fields caused the *Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety* (BMUB) to publish a circular in which the use of electronic personal dosemeters in pulsed radiation fields was prohibited. As it is, however, necessary (in particular for monitoring compliance with the dose limits in the case of pregnant women) to measure the dose with a direct-reading dosemeter, this caused problems in hospitals. Here, pregnant women were no longer allowed to work in control areas with pulsed radiation, as no suitable measuring instruments were available.

Figure 1: Typical place of use of personal dosemeters in the medical sector of X-ray diagnostics. The prescribed location for wearing dosemeters is under the protective clothing. In the area of the dosemeter, the protective apron is therefore shown transparently.

First test facility for pulsed X-radiation worldwide

As tests or requirements have so far not existed for dosemeters – neither at the national nor at the international level – it was absolutely necessary for PTB to take action. Thus, in cooperation with the Siemens company, a new facility has been developed which will, for the first time, make the testing of dosemeters for measurements in pulsed radiation fields possible.

In the case of the installations in the medical sector, the parameters of the radiation pulses are not adjusted in physical quantities like tube current or tube voltage, but according to the required image quality. This is why the challenge for the development of the appropriate test facility was to make the physical parameters which are

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required for the examination of dosemeters – independently of each other – adjustable. The thus evolved installation is the first and only facility worldwide to permit this [2].

With the reference radiation facility developed, all physical parameters of the radiation pulse – tube current and tube voltage, pulse duration and repetition rate – can be adjusted almost independently of each other. Thereby, a special rotating anode X-ray tube is used. The tube current – and thus the ionizing radiation – is switched on and off by a grid inside the tube. During that time, the high voltage is applied continuously, which is called "grid-controlled pulsing". This has made it possible to generate radiation pulses with very short rise and fall times around 50 µs and pulse durations of only 0.2 ms up to continuous operation. The adjustable tube high-voltage lies in the range from 40 kV to 125 kV; the tube current can be selected in the range from 0.5 mA to 800 mA. For electrical powers of up to 4 kW, continuous operation is possible; beyond that, only (short-term) pulsed operation is possible. In the case of the maximally possible power of 80 kW, the maximum pulse duration still amounts to 300 ms. The fact that the facility is able to generate continuous radiation is necessary for the metrological comparison with the previous testing facilities and the primary standards of PTB. The pulse repetition rate can be up to 100 Hz. A more detailed description of the facility can be found in [2].

Test requirements for pulsed radiation

The second important step was the international determination of test requirements for radiation protection dosemeters in IEC standards and of corresponding reference or test fields in ISO standards. For both tasks, Germany submitted standardization proposals, which were supported by the programme "Innovation with Norms and Standards (INS)".

To make sure that radiation protection can also be guaranteed in pulsed fields of ionizing radiation, industry has already started to develop new electronic dosemeters, and PTB is involved in developing the respective standards within IEC and ISO. The IEC/TS 62743 [3] was, for example, drawn up under the auspices of PTB. The testing of the requirements to be met here can be found in Zutz et al. [4]. At present, the technical specification ISO/TS 18090-1 for the determination of the characteristics of reference fields of pulsed radiation is being worked out under the auspices of PTB.

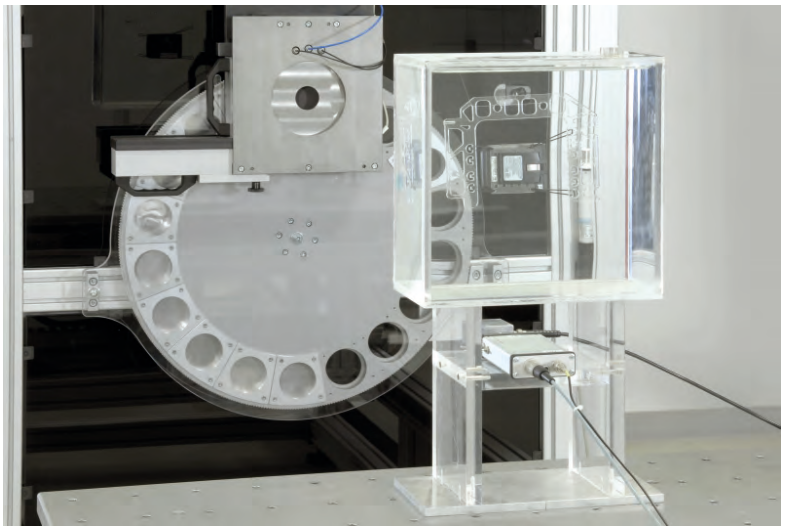

Figure 2: Facility for the generation of pulsed reference radiation (GESA). In front of it, an electronic personal dosemeter with an ISO cuboid water phantom has been installed. The time curve of the radiation pulse is measured with the monitor diode applied below it.

Transitional solution concerning pulsed radiation

Until suitable measuring instruments will be available, radiation protection must, however, also be ensured. Therefore, PTB has carried out investigations on the only electronic personal dosemeter presently available which is suitable for medical radiation fields as far as the rated range of the energy is concerned. It turned out that significant mismeasurements have already occurred at a pulse dose rate above 1 Sv/h. These dose rates are not, however, reached in "accident-free" routine operation, as the staff member stays only in the field of scattered radiation and wears protective clothing which attenuates the radiation. The dosemeters must be worn under the radiation protection clothing to correctly measure the exposure. Reliable measurements must, however, also – and in particular – be guaranteed for the case of an accident, even if an accident is improbable.

As a temporary measure, the dose rate alarm of the electronic personal dosemeter can be used as an indicator of a possible mismeasurement. For this purpose, the set value must be calculated from the parameters of the radiation field and of the dosemeter in accordance with a method described by Ambrosi et al. [5]. As soon as the alarm is triggered, the passive official personal dosemeter must be immediately evaluated for correct dose determination.

The procedure proposed has been verified by Klammer et al. [6] in measurements carried out at the above-described reference radiation facility at PTB. After that, the BMU wrote another

circular in 2011, permitting the use of this special personal dosemeter in hospitals under the conditions mentioned and under some complementary conditions.

For area dosimetry, the problems of correct measurements in pulsed radiation fields remain, however, unsolved. Here, the experts must, for the time being, rely on their expertise to detect a possible mismeasurement of the dosemeter used. Measurements in pulsed radiation fields can, for example, be checked for plausibility by variation of the distance and application of the $1/r^2$ law. Here, suitable dosemeters are urgently required.

PTB, in turn, is ready to test the first electronic dosemeter which is suitable for pulsed radiation!

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Measurement of the Radiation in the Accelerator Therapy Room

Hayo Zutz*

Motivation

In tumour radiation therapy, the use of modern linear accelerators is constantly increasing. On the one hand, the high photon energies used offer a great number of advantages for the therapy. On the other hand, they require increased precautions for radiation protection.

In the direct beam of the accelerators, the photon energies lie in the range of a few mega-electron volts. Therefore, a lot of material – i.e. thick walls with the highest possible density (e.g. lead) – is required. When the therapy rooms are designed, it is ensured by means of constructional radiation protection that persons outside the therapy rooms are not endangered.

Inside the therapy rooms, the radiation field is so blocked – by the way the beam is guided and by means of diaphragm systems – that the high dose rates required for the radiation therapy occur only in the direct beam. Irradiation of the patient with this radiation field is performed after a decision has been made as to which treatment is justified under medical aspects in the individual case. For reasons of radiation protection, persons other than the patient are not allowed to remain in the therapy room during the irradiation. This applies even if their staying would be desirable to attend to the patient.

The high-energy photon radiation is generated in the accelerator head as bremsstrahlung at a target which is bombarded with a high-energy electron beam. This intensive bremsstrahlung leaves the accelerator head as useful radiation, through a diaphragm system. A part of the developing radiation does not leave the target in the direction of the direct beam but is scattered radiation which, for reasons of weight, can be shielded only partly in the accelerator head. For complete shielding, much more shielding material would be required. This scattered radiation is also called "leakage radiation of the housing" [1]. When the direct beam is collimated to the tumour area to be irradiated, scattered radiation also develops in the diaphragm system. Ultimately, scattered radiation is generated everywhere where the direct beam hits matter.

The many sources for scattered radiation lead to a complex and intensive scattered radiation field in the entire therapy room. Due to the energy losses which occur during the scattering processes, the energy of the scattered radiation is lower than that of the direct beam. At the same time, additional electrons develop in the scattered radiation field during the scattering processes. As a result of the high direct beam energies (> 10 MeV), also neutrons may develop by nuclear reaction processes and may also contribute to the radiation field.

The aim of the measurements presented here was to investigate and quantify the scattered radiation field at the medical accelerator facilities of PTB. The accelerator facilities are commercial linear accelerators of the company Elekta of the type "Precise" as they are also used in hospitals. The original aim was a metrological one: The task to determine, for scientific experiments, the scattered radiation which originates from a phantom in the beam, compared to the scattered radiation which exists without a phantom. Then, the measurements were slightly extended to include also those positions in the room where an assisting person might possibly be located (e.g. to observe a patient during the irradiation or to reach him/her quickly). As already mentioned, this is, however, prohibited for reasons of radiation protection. The orientation measurements presented here refer only to the dose contributed by the photon fraction of the radiation field. The neutron fraction which, in the case of higher direct beam energies, occurs in addition and may also be relevant to the dose due to the higher biological effectiveness of neutrons, is not taken into account. Under technical aspects, a measurement of the dose contributed by neutrons is complicated due to the unknown energy distribution and, thus, leads to large uncertainties. There are, however, calculations and

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measurements of other groups available (see, e.g., [2]).

Measuring instruments

The measurements were carried out by means of secondary standard ionization chambers and with measurement technology especially developed at PTB (see Figure 1 and the article "Dosimetry with Ionization Chambers in External Radiation Therapy " in this publication). In order to avoid the known problems of the widely applied and easily usable electronic dosemeters, ionization chambers were used. Electronic dosemeters which are based on the counting of detector impulses may provide incorrect measurement results in the fields of the accelerators which generate pulsed radiation [3] (see also the article "Electronic Dosemeters for Pulsed Radiation" in this publication).

A particularity of a secondary standard ionization chamber is the low dependence of the response on the photon energy. This is of particular importance for the measurement of the scattered radiation field because here, photons with an unknown energy distribution – i.e. an unknown spectrum – occur. The ionization chambers used have all been traceably calibrated to the primary standard of PTB.

For the measurement of the ambient dose equivalent $H^*(10)$, an $H^*(10)$ secondary standard ionization chamber with a volume of 1 l ($H^*(10)$ chamber) was used (see Figure 1). For the measurement of the personal dose equivalent $H_p(10)$, an $H_p(10)$ secondary standard ionization chamber ($H_p(10)$ chamber) was used (see Figure 2). In addition, a personal dosemeter was used which has already proved its general suitability for measurements in pulsed radiation fields in other tests: the DIS-1 dosemeter, based on the Direct-Ion-Storage Principle [4]. It has a rated range of the photon energy from 10 keV to 7 MeV. For the measurements, this personal dosemeter was positioned on a phantom. The dosemeter concerned is an electronic personal dosemeter which is not, however, based on a counting measurement principle (see the article "Electronic Dosemeters for Pulsed Radiation").

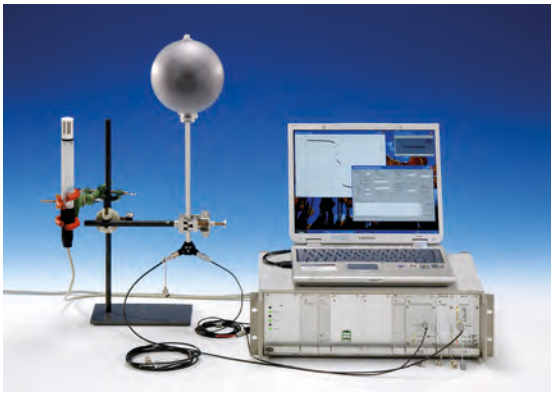

Figure 1: $H^*(10)$ secondary standard ionization chamber with measuring assembly

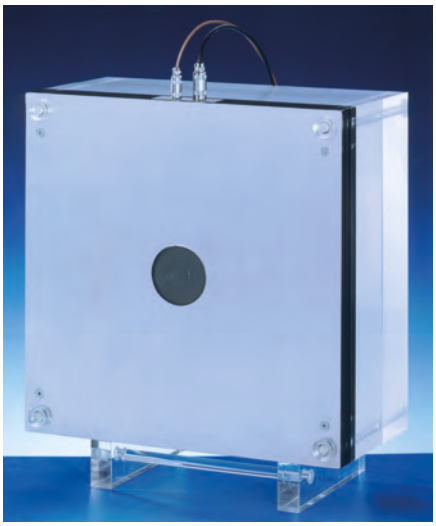

Figure 2: $H_p(10)$ secondary standard chamber

Measurements with the direct beam blocked

To investigate the scattered radiation field, the direct beam was, in the first step, blocked as far as possible with the diaphragm system. The diaphragm system is composed of two components: The Multi-Leaf Collimator (MLC), which consists of single lamellas and, thereby, allows an almost arbitrarily formed direct beam to be generated, and a pair of diaphragms which generate a rectangular field. Maximum direct beam blocking was achieved when both the MLC and the diaphragm pair were adjusted to the smallest possible field. For technical reasons, a small residual gap remains in the case of both diaphragm systems. These two residual gaps have been positioned in such a way that they do not overlap, i.e. that the residual gap of the MLC is covered by the diaphragm pair.

In spite of the shielding by the diaphragms, a radiation field remains which was made visible with photon-sensitive area detectors (storage foils). For this purpose, an area detector was positioned directly in front of the beam outlet window of the accelerator. The result is shown in Figure 3. The two remaining apertures as well as the lamella structure of the MLC are clearly visible.

The results of the first measurement series are summarized in Figure 4. The $H^*(10)$ chamber had been positioned in such a way that its centre was at the same height as the isocentre. The isocentre is the reference point of the accelerator facility at which the adjusted field sizes are defined and around which the facility rotates when the accelerator head or the gantry rotates. The measurement point at "0 m" has a lateral distance of 1 m from the isocentre to ensure that the chamber is

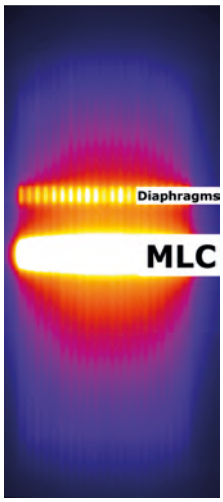

Figure 3: Storage foil image of the beam outlet window of the accelerator when the MLC (Multi Leaf Collimator) and the diaphragm system are maximally closed.

safely located outside the maximally blocked direct beam.

As can be seen, the measured dose rate decreases with the distance from the isocentre and from the accelerator head. In the case of point radiation sources, the dose rate decreases with the square of the distance r, i.e. it is proportional to $1/r^2$. In the case of the present measurements, there is no point in the irradiation room for which this dependence is valid. Consequently, there is no single point source as the main cause of the scattered radiation – there are rather several, expanded sources. In particular, the target as well as the diaphragm- and beam-guiding system are possible sources of the scattered radiation.

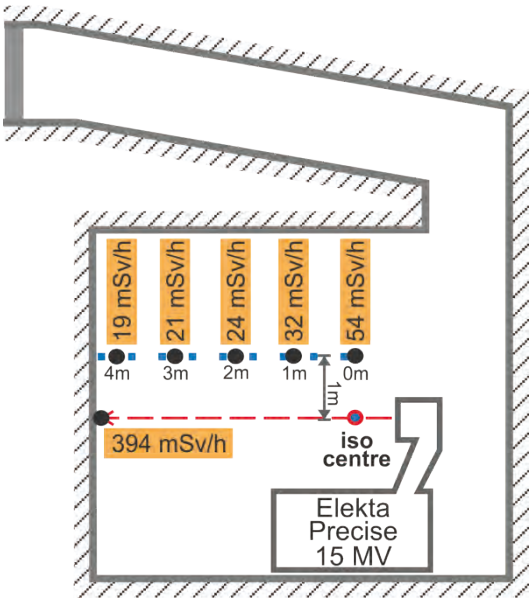

Figure 4: Time-averaged dose rate at a maximum pulse repetition frequency of 196 Hz along an axis parallel to the direct beam with the diaphragms closed.

Measurements with existing direct beam

In the second step, to assess the conditions in the irradiation room, the $H^*(10)$ chamber as well as the $H_p(10)$ chamber and the DIS-1 dosemeter were used to carry out measurements on a phantom with the diaphragm system opened and with a field size of 40 cm × 40 cm. In addition, a water phantom was placed in the isocentre which simulates a patient and is an additional source of scattered radiation. The existence of this phantom alone during the irradiation doubles the measured dose rate at the measurement points.

The results of the measurements of the personal dose equivalent, $H_p(10)$, are summarized in Figure 5. The figure represents the measured dose at the respective points with orientation of the dosemeters to the isocentre, related to the dose of 2 Gy applied in one irradiation fraction. The applied dose is measured in gray (Gy) and lies – for a patient irradiation – usually at 2 Gy per fraction. In general, several fractions are required per tumour treatment, so that the therapy will extend over several weeks if one fraction is applied per day. At the respective positions, the values measured with the DIS-1 dosemeter are – within the known measurement uncertainties (see the article "Official Personal Dosimetry for Medical Staff" in this publication) – in good agreement with the measurement data of the $H_p(10)$ chamber. In addition, the measurements of the personal dose equivalent $H_p(10)$ are in good agreement with the expectations from the measurements of the ambient dose (rate) $H^*(10)$ [5].

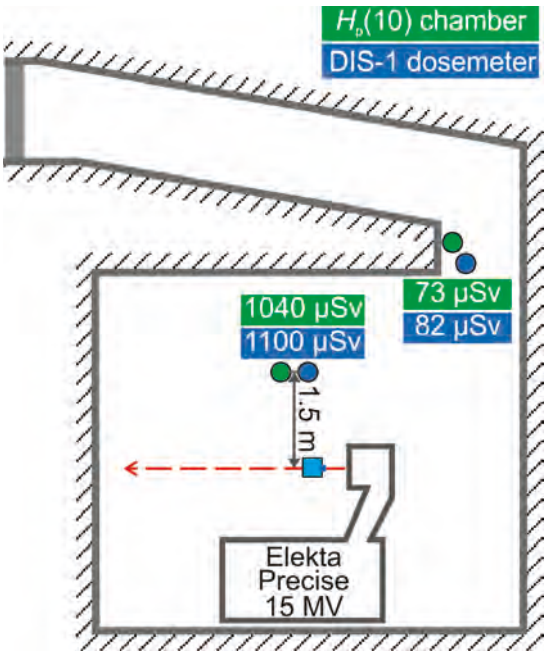

Figure 5: Measurement points in the irradiation room with indication of the personal dose equivalent $H_p(10)$ in the case of an applied dose of 2 Gy in the direct beam in the phantom, i.e., for one irradiation fraction.

To assess the measured dose values specifically in the vicinity of the water phantom, they can be compared with the legal limit values: The admissible exposure lies at 1 mSv per year for the population in general, and at 20 mSv per year for persons occupationally exposed to radiation, e.g. the MTA-R. These values can easily be reached or exceeded. Especially close to the patient, the limit value for the population in general is already reached after one single irradiation fraction with 2 Gy. These limit value considerations are not, however, valid for the patient. Here, the risk assessment is made by the physician, who will decide on the treatment that is justified in the individual case.

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Radiation Effects

Hans Rabus*

The effects of ionizing radiation on humans are of essential importance for radiation protection and radiation therapy. In both of these fields, there is a risk of a person developing cancer after healthy tissue has been damaged by radiation. This is in addition to the desired killing of cancerous tissue in radiation therapy.

The connection between the health risk incurred and the absorbed dose depends on the radiation quality (i.e. on the type of particles and on their energy spectrum). This is currently taken into account by means of so-called "radiation weighting factors" [1], where photons are always attributed the value 1, independent of the energy. It is known, however, that this value is not applicable to the "soft" X-ray range [2] and that high uncertainties are associated with the estimation of the health risk [3], especially in the low-dose range below 50 mSv. In the "Strategic Research Agenda" of the long-term Multidisciplinary European Low-Dose Initiative (MELODI), research on low-dose effects and on the fundamentals of radiation effects (both physical and biological) as a function of the radiation quality play a key role when it comes to reducing uncertainties in risk assessment [4].

The effectiveness of different radiation qualities also plays a role in radiation therapy, especially when densely ionizing radiation is used such as alpha- or Auger emitters in radionuclide therapy and in proton beams or light ion particle therapy [5]. Furthermore, it is becoming apparent (also in conventional radiation therapy) that the traditional concept of absorbed dose does not suffice as the single measurand to quantify the radiation exposure in the case of heterogeneous exposure [6]. Hence, there is a need for personalized radiation therapy, as formulated in the "Vision 2020" of the European Society for Therapeutic Radiation and Oncology (ESTRO) [7], which requires the development of metrological procedures for radiation effectiveness.

The basis for this is currently being laid, among other things, within the scope of two joint projects funded by the European Metrology Research Programme (EMRP), BioQuaRT (Biologically weighted quantities for radiotherapy) [8] and MetroMRT (Metrology for molecular radiotherapy) [9]. Procedures are therefore being developed – first, to measure the physical properties of the particle track structure of densely ionizing radiation (see the article by G. Hilgers in this publication) and, secondly, to numerically simulate the particle track structure and its effects on the genome in biological cells (see the article by M. Bug and H. Nettelbeck in this publication). The latter is made possible by measuring the interaction cross sections for the ionization and fragmentation of the components of DNA (see the article by A. Arndt and W.Y. Baek in this publication). The predictability of the biological effectiveness is based on radiobiological investigations conducted using PTB's ion microbeam (see the article by U. Giesen in this publication).

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[9] http://projects.npl.co.uk/metromrt/

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The Effect of Radiation on Biomolecules

Alexander Arndt*, Woon Yong Baek**

Investigations with regard to sub-cellular radiosensitivity, conducted using a micro-ion beam and radionuclides attached at different locations of the cell, indicate that DNA is the critical target for the radiation damage in biological systems. A large part of the radiation-induced mutagenic and lethal effects can be attributed to the structural and chemical modifications of the DNA, such as double-strand breaks and fragmentation of bases.

Different physical processes contribute to these modifications. The primary ionizing radiation may cause breaks of molecular bonds in the DNA components along its trajectory by direct excitation or ionization. A larger fraction of the radiation damage (approx. 2/3) is, however, induced by the subsequent processes which are triggered by secondary particles, such as electrons, fragment ions and reactive radicals which are generated by the interaction of the primary radiation with both the DNA and the surrounding medium. By chemical processes, the fragment ions and the radicals contribute to the modification of the DNA, whereas secondary electrons may break up the molecular bonds of the DNA through further excitation, ionization or dissociative attachment. Due to the small range of the secondary particles of only a few nanometres, these follow-up processes often lead to irreparable clustered damage in the DNA.

With the measurement methods currently available, an experimental investigation of the primary physical processes in the range of the DNA is not feasible. Monte Carlo simulations are therefore often used to assess radiation-induced damage. Despite the well-advanced development of the numerical method of Monte Carlo simulations, a large gap presently exists in the cross section data sets for the interaction between ionizing radiation and the molecular constituents of DNA.

The electron scattering cross sections of DNA components are of central importance. Large numbers of electrons are produced as secondary particles by any kind of ionizing radiation penetrating tissue. These secondary particles are responsible for the most important part of the track structure in the submicrometre range which is decisive for the relative biological effectiveness. Furthermore, recent studies have shown that even electrons with a negligibly small kinetic energy may cause strand breaks in the DNA due to dissociative attachment. In addition to the electron scattering cross sections of the DNA constituents, the cross sections for the production of fragment

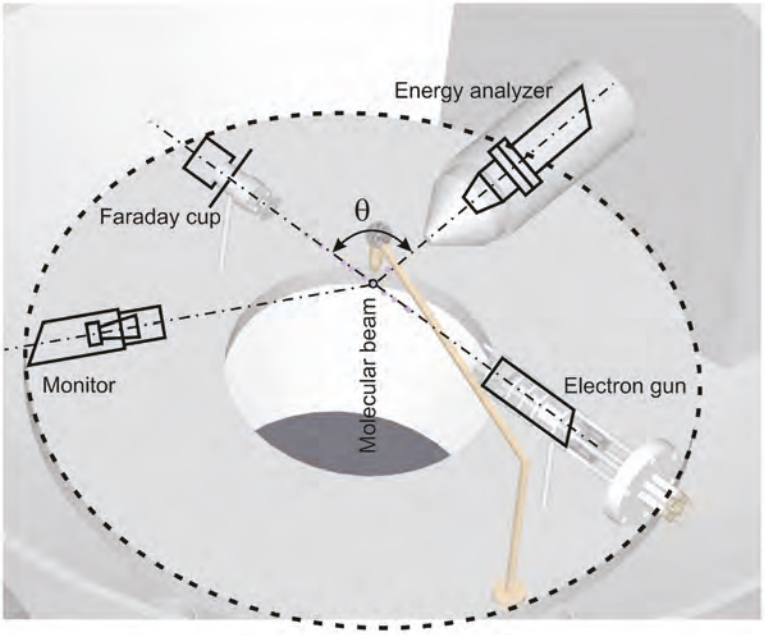

Figure 1: Schematic representation of the crossed-beam arrangement in the scattering plane. In the scattering plane, the effusive molecular beam, which moves into the drawing layer, is crossed by the electron beam. The scattered electrons are analyzed according to their energy by means of a 180° hemispherical deflector. The scattering angle is adjusted by rotating the electron gun relative to the energy analyzer. The monitor and the Faraday cup serve to monitor the flux density of the molecular beam and of the electron current.

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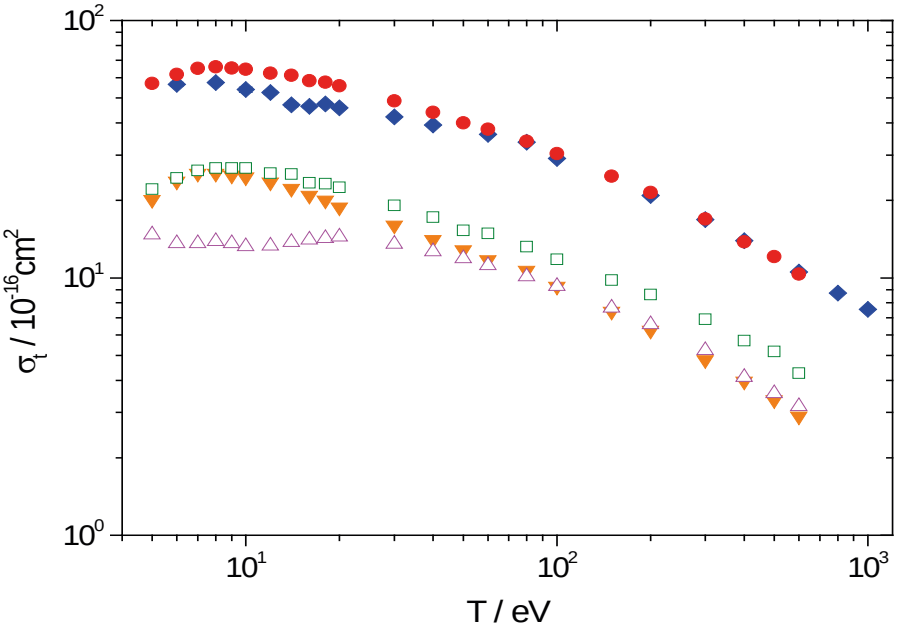

Figure 2: Total electron scattering cross sections σ_t of tetrahydrofuran as a function of the electron energy.
T: (♦) measurement results [8], (●) semi-empirical values calculated with the aid of the additivity rule, (□) σ_t of C_2H_4 [1–2], (▼) σ_t of CH_4 [3], (Δ) σ_t of CO [4–6] .

ions after electron or ion bombardment are of interest. These fragmentation cross sections not only provide information about the reaction channels which lead to the break of the bonds, but also information about the charge and mass distribution of the fragment ions which may contribute to a further modification of the DNA structure as a result of the aforementioned chemical follow-up processes.

In view of the lack of data in the literature, experiments have been developed and conducted by the "Electron Cross Sections of DNA Ingredients" Working Group. The apparatus allows the total, singly differential elastic scattering electron cross sections and the doubly differential inelastic electron scattering cross sections to be measured for primary energies from 20 eV to 1 keV. The measurable scattering angle range lies between 5° and 135°. The energy spectrum of the secondary electrons can be measured down to 3 eV. The total electron scattering cross section is determined by means of a linear transmission experiment, based on Beer's attenuation law. As schematically shown in Figure 1, the differential elastic and inelastic electron scattering cross sections are measured with a crossed-beam arrangement. The scattering angle is adjusted by rotating the electron source relative to the electron energy analyzer. In addition, a mobile measuring facility has been developed which allows the determination of the fragmentation cross sections of DNA constituents after the interaction with electrons and ions.

As an example, Figure 2 shows the total electron scattering cross sections σ_t of tetrahydrofuran (C_4H_8O) which has a molecular structure similar to that of deoxyribose – hence, its use as a substitute molecule. The data calculated semi-empirically using the total electron scattering cross sections of C_2H_4 [1–2], CH_4 [3] and CO [4–6] and the additivity rule are also shown. The good agreement between the experimental and the semi-empirical values indicates that the total electron scattering cross sections of complex biomolecules can be approximated by the sum of the total electron scattering cross sections of the individual atoms or functional groups for electron energies above approx. 20 eV. Coherent scattering, which is of relevance for electrons whose de Broglie wavelength is comparable to the molecular bonding length, plays only a minor role in the total scattering cross sections.

Figure 3 shows a comparison of the experimental differential elastic electron scattering cross sections $d\sigma_{el}/d\Omega$ of tetrahydrofuran for 80 eV electrons with theoretical values calculated using the modified independent atom model [7], which include contributions from coherent and multiple scattering inside the molecule. The broken curve represents the sum of the differential elastic scattering cross sections of the individual atoms. The significant deviation between the two curves suggests that in the case of the differential electron scattering cross sections, the application of the additivity rule is subject to a large uncertainty. The experimental determination is mandatory since a theoretical method capable of predicting differential electron scat-

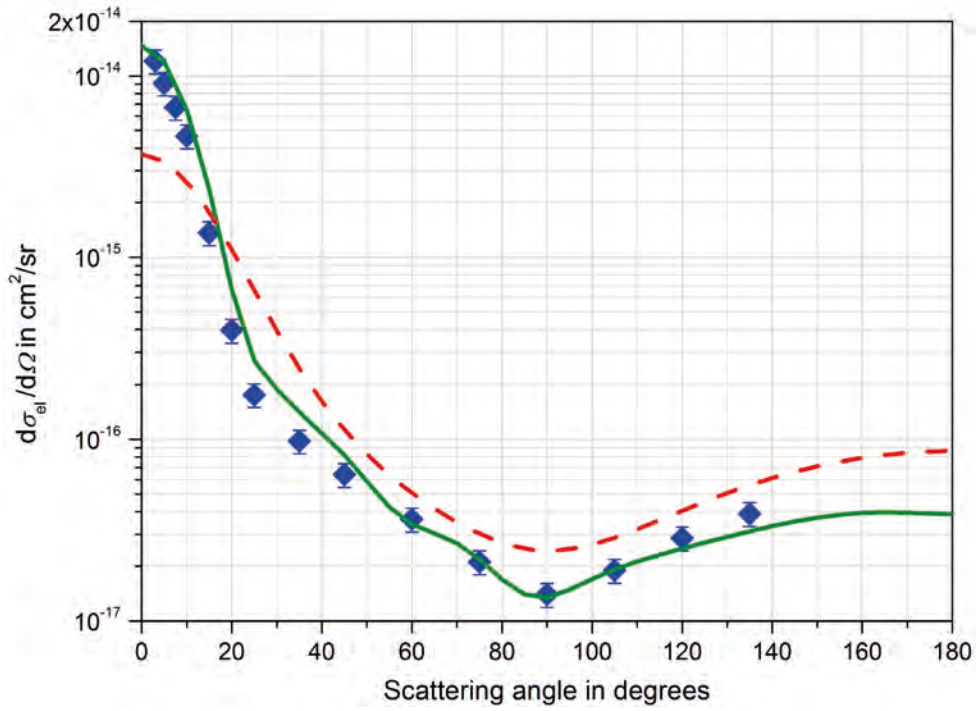

Figure 3: Differential elastic electron scattering cross sections $d\sigma_{el}/d\Omega$ of tetrahydrofuran for 80 eV electrons as a function of the scattering angle: (♦) measurement results, (–) theoretical values calculated with the aid of the modified independent atom model [7], (---) sum of the differential elastic electron scattering cross sections of the individual atoms of the molecule.

tering cross sections with sufficient accuracy is not yet available.

In addition to the direct interaction of primary ionizing particles or their secondary electrons with DNA constituents, knowledge of the molecular fragmentation processes post-ionization is also important for understanding radiation-induced DNA damage. This is because these processes provide information about the reaction channels involved in the dissociation. Although numerous experiments exist for the determination of the mass distribution of fragments, few data sets have been published for the absolute fragmentation cross sections of biomolecules after electron or ion bombardment. A facility has therefore been established at PTB with the aim of determining these data sets for DNA constituents as precisely as possible.

The measurement apparatus for the determination of the fragmentation cross sections comprises three components. The first is for sample preparation, where the sample material is expanded through an aperture of 30 µm diameter from a high-pressure reservoir (approx. 1 to 8 bar) into a rough-vacuum environment (10^{-3} mbar). This configuration leads to a supersonic expansion. In the centre of the expansion volume, the molecules are almost free from interaction and move along the expansion direction in a straight and uniform line. As most of the bio-molecular substances are available in a solid or liquid aggregate state at room temperature, the high-pressure reservoir is equipped with efficient heating elements which can be heated to a maximum of 200 °C. Hence, this preparation is limited to substances which have an evaporation temperature or boiling point below 200 °C at the given operating pressure. Using this technique, it is possible to generate a molecular beam of biomolecules.

The preparation stage is followed by the second component which contains the interaction zone. In this zone, the molecular beam crosses a beam of ionizing radiation, where the selection of the radiation source is only limited by the compatibility of the connecting flanges. A focused electron source with an energy range between 5 eV and 2000 eV, an ion accelerator delivering protons between 70 keV and 130 keV, and the accelerators of the PTB ion accelerator facility PIAF (proton energies between 400 keV and 16 MeV, He-ion energies between 1.66 MeV and 16 MeV) have been used for the measurements so far.

The interaction of ionizing radiation and biomolecules leads to ionization and fragmentation of molecules. These fragments can be detected using pulsed sources of ionizing radiation and a time-of-flight spectrometer. The spectrometer is able to record time-related fragmentation patterns up to 10 µs after the moment of interaction. Such measurements of the interaction dynamics provide the basis for determining absolute fragmentation cross sections.

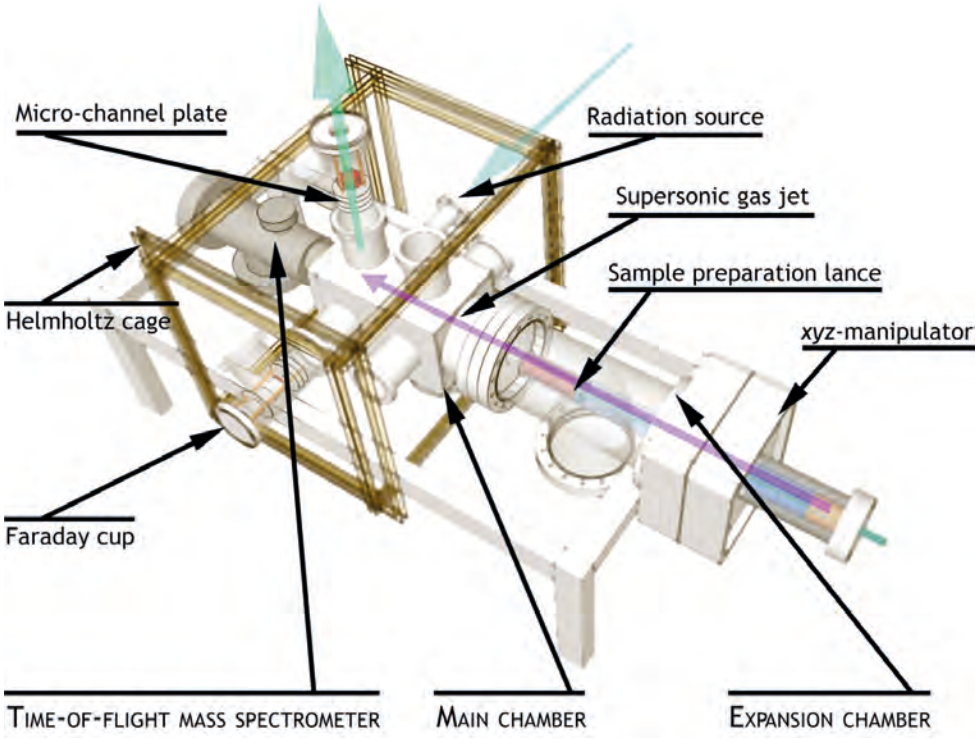

Figure 4: Schematic set-up for measuring fragmentation cross sections. The direction of motion of the molecular beam is symbolized by the violet arrow; beam directions of the ionizing radiation are indicated by green arrows. Important modules for the generation of the molecular beam and the detection of the ionizing radiation used are labelled.

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Simulation of the Radiation Effect on DNA

Marion Bug*, Heidi Nettelbeck**

The biological effect of ionizing radiation is generally initiated by energy depositions of the radiation on DNA molecules. Subsequent chemical and biological processes in the damaged cell may lead to a mutation (carcinogenesis) or to programmed cell death (apoptosis).

To assess a radiation effect on the DNA, the track structure of the relevant radiation type is simulated in segments of the DNA (Figure 1). Particle track structure simulation uses Monte Carlo procedures to reproduce the stochastic nature of radiation interaction with matter and allow a numerical solution of complicated particle transport problems to be calculated. Particle transport in microscopic volumes, such as a DNA segment of a few nanometres, is accomplished by the simulation of single interactions (i.e. event by event).

Track structure simulation allows the determination of nanodosimetric quantities, such as the ionization cluster size (see the article "Measurement of the Track Structure of Ionizing Radiation" in this publication). These quantities, which characterize the particle track structure, can be related to the initial radiation damage in molecular dimensions [1]. Hence, precise simulation of the track structure of secondary electrons is crucial as these electrons are generated in large numbers when ionizing radiation passes through matter. Such detailed simulation requires interaction cross sections to describe the probability for a specific interaction of the incident particle with the bonded electrons of DNA molecules. Cross sections of the DNA are often substituted by those of water, as a complete data set for the molecular components of DNA is lacking in the literature.

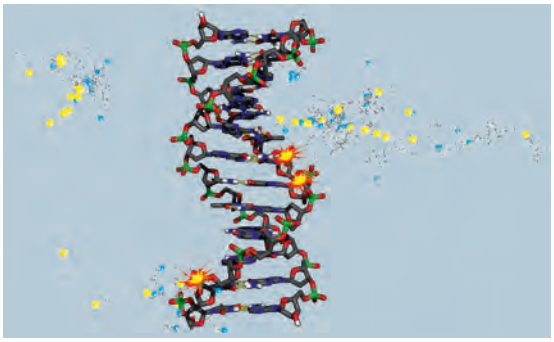

Figure 1: Simulated electron track in water and DNA. The dots represent positions of individual interactions in water and indicate the type of processes (ionization: yellow; electronic excitation: blue; elastic scattering: grey). Ionizations on the DNA are represented by flashes.

The DNA comprises a total of six molecular components: the sugar deoxyribose and a phosphate group, which occur in alternating sequence in the polymer strings forming the "backbone" of the DNA double helix, and four nucleobases which are bonded in pairs to opposite sugar molecules. The nucleobases, which occur in a non-periodical arrangement, encode the genome. The "pairs" consist of one of the purine bases adenine or guanine and one of the pyrimidine bases cytosine or thymine. For simulation of the radiation effect on DNA, the basic components purine and pyrimidine can be regarded as model molecules for the respective nucleobases, while the molecule tetrahydrofuran is a molecular substitute for deoxyribose.

Data were measured at PTB (see the article "The Effect of Radiation on Biomolecules" in this publication) for the two DNA components tetrahydrofuran (THF) and pyrimidine (PY). Measured differential cross sections were interpolated and extrapolated for small and large scattering angles and then subsequently integrated. The cross section data of the phosphate group and purine bases were assessed with the aid of theoretical models.

For electron transport in DNA, relevant cross sections are converted into probability distributions and the following steps are simulated. In the first simulation step, the path length of the electron to its next position of interaction is determined from the total scattering cross section of a nucleotide (a nucleotide consists of THF, a phosphate group, a nucleobase and water molecules stored in the DNA helix) and the number density of the nucleotides in the DNA. For a cylindrical volume of 2.3 nm in diameter and 3.4 nm in height, the number density is 20 nucleotides. In the subsequent simulation step, a specific DNA molecule is selected for the interaction using the total scattering cross sections of the single molecules. These total scattering cross sections depend on both the

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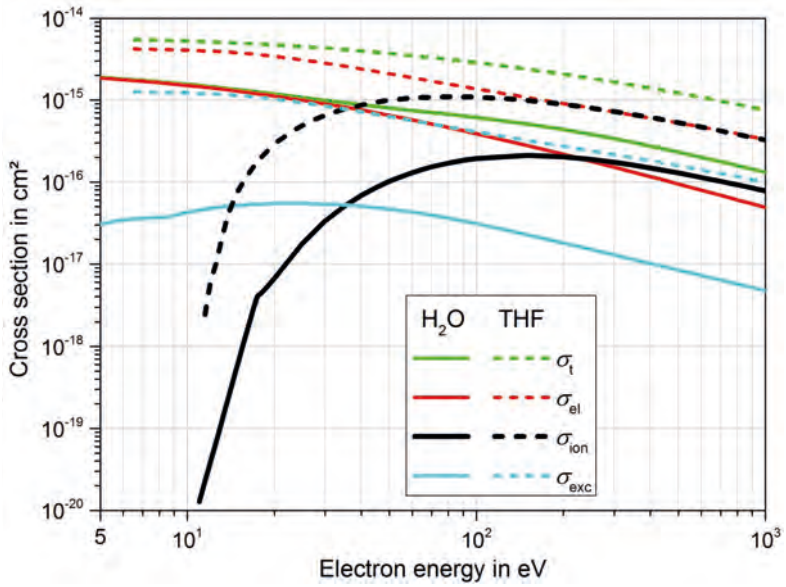

Figure 2: Cross sections for the interaction of electrons with water and THF: Total cross section (σ_t) as well as cross sections for elastic scattering (σ_{el}), ionization (σ_{Ion}) and excitation (σ_{exc}).

electron number and spatial size of the molecule. Hence, the electron has a higher probability of interacting with a DNA molecule than with water (Figure 2).

The next simulation step is concerned with determining the type of interaction for the selected molecule using the total cross sections for elastic scattering, electronic excitation and ionization. In the case of elastic scattering on the molecule, the electron undergoes a change in direction and the corresponding scattering angle is defined by the differential elastic scattering cross section. Energy depositions in the molecule arise from an excitation or ionization. In the case of an ionization, the incident electron additionally transfers energy to a secondary electron. The secondary electron energy, the deposited energy and the respective scattering angles are determined from the differential ionization cross sections. Each electron is transported until its energy falls below the ionization threshold of the DNA molecules (9.6 eV), where it is assumed that it locally deposits its complete residual energy.

The distribution of ionization cluster sizes is obtained from a simulation of the track structure for a large number of incident electrons. This quantity can then be used to assess a biological radiation effect, such as determining the probability of a double-strand break (DSB), where lesions occur on opposite strands of the DNA. For DSBs, a combinatorial model has been developed [2] which is based on the assumption that the transformation of an ionization into a lesion is described by a constant probability p_c. This probability has been determined from biological experiments to be 11.7 % [2]. The conditional probability to transfer an ionization cluster size of ν into a DSB is thus

$$P(DSB\,|\,\nu) = 1 + (1-p_c)^{\nu} - 2\left(1-\frac{p_c}{2}\right)^{\nu} \qquad (1)$$

The convolution of equation 1 with the distribution of the ionization cluster size $P(\nu|T)$, which was obtained from the simulation of electrons with the initial energy T, yields the following probability to produce a DSB:

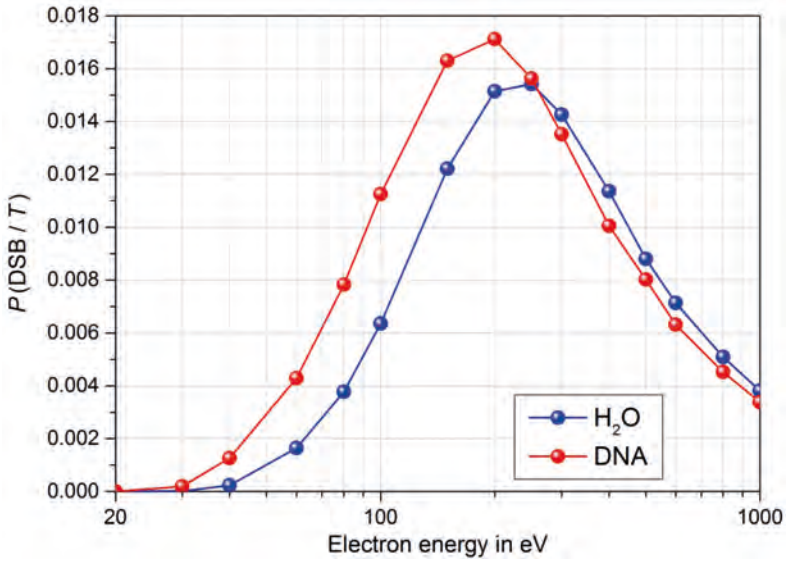

Figure 3: DSB probabilities as a function of the electron energy for simulations in water and DNA.

$$P(DSB\,|\,T) = \sum_{\nu=2}^{\infty} P(DSB\,|\,\nu)\;\; P(\nu\,|\,T) \qquad (2)$$

Figure 3 shows the probability for electrons to generate a DSB when passing the DNA. These results were obtained from simulations performed in a medium consisting of either DNA molecules or liquid water. The good agreement of DSB probabilities in both media for electrons with energies above 250 eV suggests that water is a realistic model for the DNA in this energy range. Below this energy, the maximum DSB probability for electrons with energies around 200 eV is as much as 30 % larger when cross section data of DNA molecules are used instead of those for water. For 30 eV electrons, this difference is only 6 %.

The effect of radiation on DNA can be estimated by the determination of nanodosimetric quantities when ionizing radiation passes through DNA. Results obtained with realistic simulation of the DNA, made possible by the measurement of a complete set of cross sections of DNA molecules at PTB, indicate an underestimation of the radiation effect when – as per conventional practice – water is used as a substitute for DNA.

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Measurement of the Track Structure of Ionizing Radiation

Gerhard Hilgers*

1 Introduction

For the biological and physiological effects of radiation exposure, the stochastic nature of the radiation interaction plays a decisive role, especially with DNA as the carrier of the genetic information. The aim of nanodosimetry is to create a metrological basis for the concepts describing the radiation effect, which is based on the physical characteristics of the microscopic track structure of ionizing radiation particles. The term "particle track" thus denotes the sequence of interaction sites of a primary particle and any secondary particles, including radiation effects. Taking the particle track structure into account is particularly important in the case of ion beams, where the macroscopic dose distribution is mainly concentrated along the primary particle tracks.

2 Nanodosimetric measurands

In nanodosimetry, the ionization component of the particle track structure is of importance, which is characterized by the relative frequency distribution of the ionization cluster size. Ionization cluster size is the number ν of ionizations generated in a defined (generally cylindrical) target volume by a primary particle and its secondary electrons. A primary particle of radiation quality Q can either traverse the target volume or pass it at a distance d relative to the longitudinal axis of the cylinder (Figure 1). The ionization cluster size ν can be interpreted as a superposition of the ionization component of the particle track structure and of the geometric characteristics of the target volume. The ionization cluster size distribution is characterized by the statistical distribution of the probabilities $P_\nu(Q,d)$ (which is normalized according to equation (1)) that exactly ν ions are created in the target volume.

$$\sum_{\nu=0}^{\infty} P_\nu(Q,d) = 1 \qquad (1)$$

For the characterization of the particle track, the statistical moments of the probability distribution are also suited. Of particular interest is the first moment of the distribution, this is the mean ionization cluster size $M_1(Q,d)$, which is calculated according to equation (2).

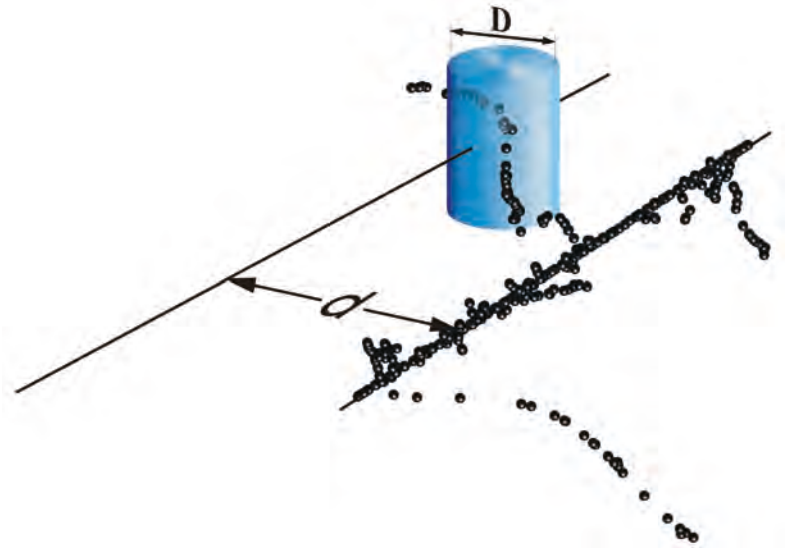

Figure 1: Generation of an ionization cluster by an ionizing particle passing a cylindrical target volume of diameter D at a distance d from the cylinder axis. The shown segment of the particle track represents the ionization component of the track structure.

$$M_1(Q,d) = \sum_{\nu=0}^{\infty} \nu \cdot P_\nu(Q,d) \qquad (2)$$

The ionization cluster size distribution $P_\nu(Q,d)$ depends not only on the radiation quality Q (i.e. the type of primary particle and its energy) but also on the geometry of the target volume and its material composition and density.

The principle of density scaling (see Section 4) can be applied to various material combinations of density and target volume dimensions for which one obtains approximately the same ionization cluster size distributions. This enables a direct experimental determination of ionization cluster size distributions in biologically relevant targets, such as the DNA, by conducting measurements with diluted gases in macroscopic volumes. In this case, the particle density is adjusted via the gas pressure in such a way that the measured ioniza-

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tion cluster size distribution corresponds to that expected in a short segment of two turns of the DNA double helix or ten nucleic base pairs. This target size is relevant for radiation biology, as an accumulation of damage (such as that caused by ionization) in such a short DNA segment is known to lead to a so-called complex "double-strand break" (DSB). Additional strand breaks within the DNA segment renders the repair of this break difficult and often incomplete. This leads to either programmed cell death or the generation of radiation-induced cancer.

3 Experimental nanodosimetry

The nanodosimeter operated at PTB was developed in cooperation with the *Weizmann Institute of Science* in Rehovot, Israel [1,2]. Figure 2 shows the basic set-up for measurements carried out with the PTB nanodosimeter at an ion accelerator. To reduce the primary particle rate, the ion beam strikes a thin gold foil in a scattering chamber attached to the front of the nanodosimeter. By means of Rutherford scattering, a small number of ions are scattered horizontally at an angle of 45° towards the entrance aperture of the nanodosimeter or at an angle of –45° on a semiconductor detector which monitors the energy spectrum of the scattered particles. A thin Mylar foil separates the high vacuum of the scattering chamber from the nanodosimeter. In the ionization volume of the nanodosimeter, which is located between the electrodes of a parallel-plate capacitor, there is a gas pressure of approximately 100 Pa. When an ion enters the ionization chamber through the entrance aperture, it traverses the chamber parallel to the two electrodes before it is registered in a semiconductor detector behind the exit aperture. Due to the applied electrical field, the ionized gas molecules generated along the primary particle track drift toward the lower electrode. Ions which are generated in the sensitive volume above a small aperture in the lower electrode are extracted from the ionization volume through the lower electrode and then transported through an ion optics to a photomultiplier tube, where they are detected.

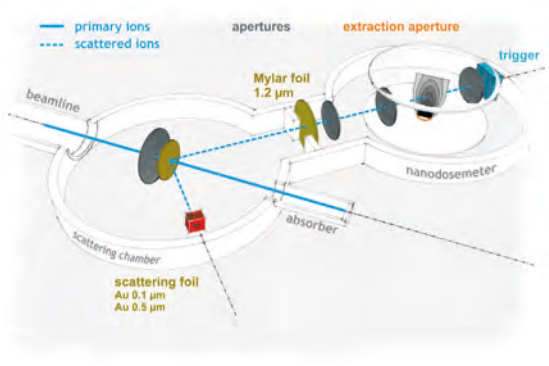

Figure 2: Schematic setup of the experiments carried out with the PTB nanodosimeter [3].

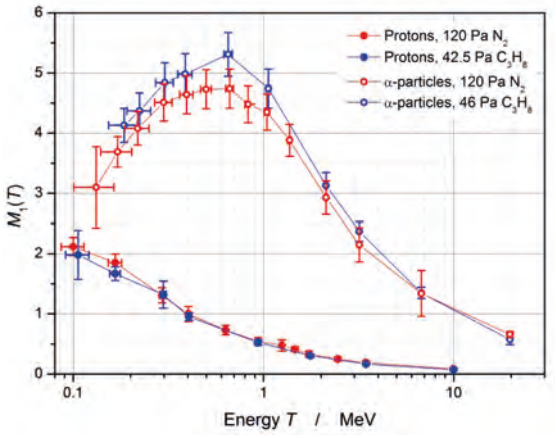

Figure 3: Mean ionization cluster sizes $M_1(T)$ for alpha particles and protons of various energies for (120.0 ± 1.2) Pa N_2 and (42.5 ± 0.4) Pa C_3H_8 (protons) or (46.0 ± 0.5) Pa C_3H_8 (alpha particles).

4 The scaling method of nanodosimetry

The nanodosimeter is used to measure ionization cluster size distributions of a diluted gas in a macroscopically sensitive volume with dimensions of the order of 1 mm. This volume contains approximately the same number of gas particles as a volume with 1 nm dimensions and a density similar to that of liquid water (approx. 1 g/cm^3). The principle of density scaling in nanodosimetry also takes into account the ratio of the mean free path lengths of the ionizing particles in the respective medium [4], which are inversely proportional to the cross section for ionization. Consequently, equivalent ionization cluster size distributions should be obtained if the following relation is valid:

$$(D\rho)^{(Gas)} = (D\rho)^{(Water)} \frac{(\lambda\rho)_{Ion}^{(Gas)}(Q)}{(\lambda\rho)_{Ion}^{(Water)}(Q)} \qquad (3)$$

where D is the diameter of the target volume, ρ is the mass density and λ_{Ion} the mean free path length for ionization by a particle of radiation quality Q.

To verify the validity of equation (3) independent of the radiation quality and materials used, ionization cluster size distributions were measured in the nanodosimeter for monoenergetic proton and alpha particle beams of energies 0.1 MeV to 20 MeV. Propane (C_3H_8) and nitrogen (N_2) were the filling gases in the nanodosimeter. Figure 3 shows the mean ionization cluster sizes calculated from the measured cluster distributions in the sensitive volume as a function of the primary particle energy.

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Radiation Effects at the Cellular Level

Ulrich Giesen*

1 Introduction

When using ionizing radiation in medicine, there are two extremes for the desired radiation effects. On the one hand, the high-dose range in radiation therapy which is aimed at damaging and killing the cancer cells as much as possible. And on the other hand, the low-dose range in X-ray and CT diagnostics where, in the ideal situation, no radiation effects on cells are desired. Both extremes can, unfortunately, not be fully attained. The maximum radiation dose in the tumour is limited by the side-effects in the surrounding healthy tissue, which is also irradiated. By using sophisticated irradiation methods and selecting different radiation qualities – loosely ionizing gamma or proton radiation or densely ionizing heavy-ion radiation – the attempt is made to maximize the impact in the tumour whilst minimizing the effects on the healthy tissue. However, there always remains a low-dose zone outside the tumour volume.

The biology of radiation effects (i.e. radiation biology) is one of the bases of radiation therapy. The objective of investigating radiation effects at the cellular level is, among other things, to quantify and to improve the understanding of the relative biological effectiveness (RBE) of different types of radiation (see Section 2 of this article) and, for low doses of radiation, to decipher the underlying biological mechanisms in order to improve the risk assessment for cancer due to radiation damage. For this purpose, PTB operates, among other things, a charged-particle microbeam (see section 3 of this article) to irradiate live cells with protons or alpha particles. These interdisciplinary research activities are carried out within the scope of collaboration projects with radiation biologists from Germany and elsewhere in Europe, partly with funds from European research programmes.

The effects of low doses of radiation are also of consideration for the radiation protection of the medical staff during radiation therapy, X-ray diagnostics and the administration of radiopharmaceuticals, but also for other professional groups and other sections of the population who might be exposed to natural radiation sources such as, e.g., cosmic radiation or the radon gas released from the ground. For the health hazard caused by low doses of radiation, i.e. lower than 50 mSv, there are hardly any reliable data and estimations. Research on radiobiological phenomena in the low-dose range (e.g. bystander effects [2], [3]), nano-dosimetry and multiscale modelling play key roles in the research programmes of BMU and the EU as well as in the long-term EU initiative MELODI [1].

2 The relative biological effectivenesses of X-ray, gamma and particle radiation

The biological effectiveness of the different types of radiation depends on the type and on the energy of the radiation in question. For therapeutic effects and for a better assessment of health risks due to radiation, an important pre-condition is not only to exactly measure the radiation dose, but also to have a good knowledge of the underlying biological effects.

For radiation therapy, the effect of loosely ionizing electron, gamma and X-ray radiation – as applied in conventional radiation therapy and X-ray diagnostics – is the reference point with a *relative biological effectiveness: RBE* = 1 and, for radiation protection, with a radiation weighting factor $w_R = 1$, respectively. Densely ionizing radiation has a greater radiation effect for the same physical dose; it increases along with the physical parameter *"linear energy transfer": LET*, which reaches a maximum around 100 keV/µm.

The clinical RBE values in the tumour volume lie around 1.1 for proton therapy and around 3 for heavy-ion therapy with carbon ions [4]. In general, the RBE, however, depends on the dose, on the particle energy and on the penetration depth. It is partly based on in-vitro measurements of survival curves of various cell lines. The European consortium BioQuaRT (*Biologically weighted quantities in radiotherapy*) was created to improve the understanding of the RBE and its comparability; with funds from the EU's EMRP programme, it develops new measurement methods and new simulation techniques. At PTB's microbeam (see section 3 of this article), radiation biologists from France, Italy and Portugal measure early and late

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radiation effects in cell cultures. The results are then used as input and benchmark data for further model computations.

In radiation protection, the radiation weighting factors w_R for the different types of radiation are based on evaluations which take into account the type of irradiation (internal/external) as well as epidemiological studies and the RBE factors from cell experiments at low doses [5]. There are different RBE factors for different radiation effects in the investigated cells (so-called "end points": survival, mutation, formation of dicentric chromosomes, etc.), but also for different types of cells (lymphocytes, tissue cells, tumour cells). As an example, Fig. 1 shows the survival curves of human CGL1 cells for gamma and alpha radiation (University of Göttingen) and for neutrons (PTB) [6].

In cooperation with GSF (new name: Helmholtz-Zentrum München, the German Research Center for Environmental Health), BfS (Federal Office for Radiation Protection) and LMU Munich, the radiobiological effects of neutrons

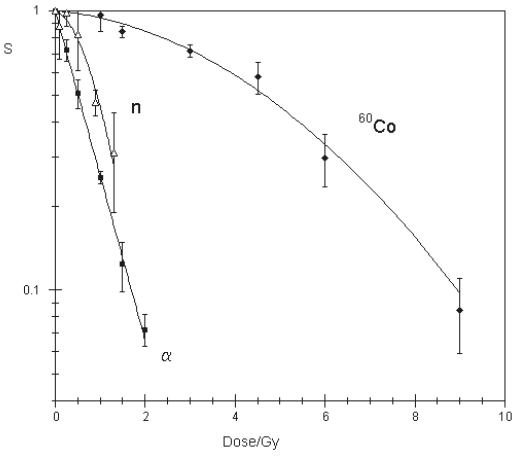

Figure 1: Survival rate of human CGL1 cells as a function of the absorbed dose after being irradiated with ^{60}Co gamma radiation, 3.4 MeV alpha particles and neutrons with an energy of 0.565 MeV, respectively.

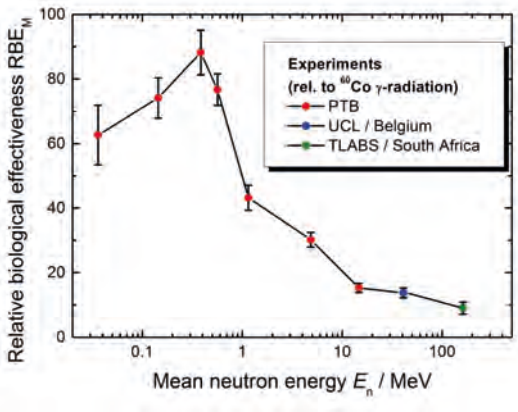

Figure 2: Relative biological effectiveness of neutron radiation as a function of the neutron energy related to ^{60}Co gamma radiation.

were also determined by the frequency of induced chromosome aberrations. Human lymphocytes were irradiated with neutrons over a large range of energies (30 keV – 15 MeV at PTB, Germany; 60 MeV at UCL, Belgium; 200 MeV at TLABS, South Africa. The results of these measurements (Fig. 2) [7], [8] were taken into account in the international recommendations for the radiation weighting factor for neutrons [5].

3 Radiobiological investigations at PTB's ion microbeam

PTB's excellent radiation sources for α-, β-, γ-, X-, ion and neutron radiation are the precondition for the exact determination of the radiation dose and for the calibration of dosemeters in the different radiation qualities. In addition, they also provide a special infrastructure to investigate the biological effects of radiation. Especially the neutron fields are, at least for Germany, unique.

At the PIAF accelerator facility (PTB Ion Accelerator Facility, see Fig. 3), protons, deuterons and alpha particles with energies from 0.1 MeV to 27 MeV are generated by means of a 3.75 MV (million volt) van de Graaff accelerator and with a compact cyclotron. These are used either directly for radiation physics (measurements of: W values of ions for particle therapy, ionization cluster distributions for nanodosimetry, characterization of particle detectors) or for the production of monoenergetic neutron fields or high-intensity neutron beams with a broad energy distribution by nuclear reactions of the ions with certain materials.

The ion microbeam (see Fig. 4) was mainly developed for radiobiological investigations, but also to measure effects in electronic circuits and detectors [9]. This facility allows ion beams to be focussed to a few thousandths of a millimetre and individual cells (cell nucleus or cell plasma) to be irradiated selectively with an accuracy of approx. 2 µm. The number of particles per cell is

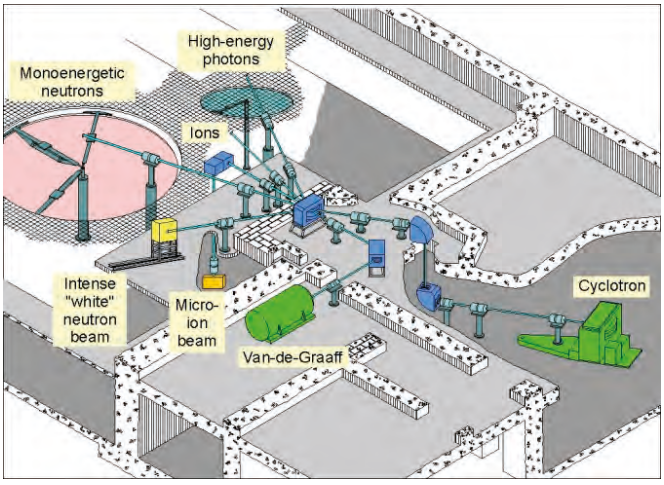

Figure 3: Overview of the PIAF accelerator facility.

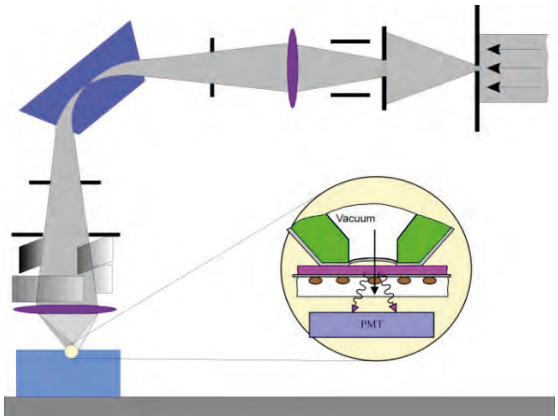

Figure 4: Schematic set-up of the ion microbeam.

controlled accurately by a fast deflector. Therefore, at the microbeam, any cell nucleus or a selection of cells is hit, for example, by exactly one alpha particle – or by a defined number of alpha particles, as desired. In addition, the use of different ions and ion energies enables us to study the effects of different radiation qualities. Alpha particles with a high LET of about 100 keV/µm are used to investigate the impact of densely ionizing particles such as, e.g., the alpha particles that occur in radon decay. In contrast to this, energetic protons allow the impact of loosely ionizing radiation such as, e.g., X-rays with a low LET from approx. 3 keV/µm to 20 keV/µm, to be investigated.

In a radiobiological lab which is located near the accelerator facility, the radiation biologists prepare the cells and typically seed 2,000 to 10,000 cells in special dishes in a monolayer. At the microbeam, all cells on these dishes are identified and their position is determined with the aid of a microscope. After having been irradiated with the desired number of particles, the cells are cultivated further, and the radiobiological endpoints – such as the cell survival curves or the chromosome aberrations due to wrong DNA repair – are analyzed by the biologists.

It is not yet fully understood how the first steps of DNA damage detection take place inside the cells. In an interdisciplinary cooperation project between PTB, the *German Collection of Microorganisms and Cell Cultures* (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH – DSMZ, Braunschweig) and the *University Hospital of Düsseldorf*, the new method of "live-cell imaging" was established at the microbeam [[10], [11]]. Along particle tracks, double-strand breaks (DSBs) occur which – within seconds and minutes – trigger a variety of reactions and DNA repair processes in the cells. These initial responses can now be observed "live" with a microscope as the appearance of fluorescent foci (along the particle tracks), because the cells have been genetically modified by fusing, for example, the green or red fluorescent protein (GFP or RFP) with a selected reporter or repair protein which then accumulates at the DSB's (see Fig. 5).

Within the scope of the cooperation project, experiments with a selection of fluorescence-labelled repair proteins are carried out. The partners from the DSMZ and the University Hospital of Düsseldorf managed to engineer these fused proteins, to insert them into a human cell line and to achieve stable expression. Thus, different processes and repair pathways can be selectively investigated as a function of the dose (number of particles), of the radiation quality and of the LET. Besides the spatial processes, also the time-dependent processes are analysed (see Fig. 6), and it becomes possible to find out which proteins bind first to the double-strand breaks and how these dynamic processes of damage detection and repair differ from one type of particle and energy (LET) to the other.

Cell irradiations at the microbeam are also used to investigate how drugs could influence damage detection and repair. What we are looking for are substances which make cancerous cells more sensitive selectively or which improve repair in healthy tissue cells. Identifying and characterizing so-called "radioprotectors" and "radiosensitizers" are active research fields for radiation therapy, but also for manned space research.

By irradiating cells in monolayers at the microbeam, important phenomena of radiation effects can be investigated and basic mechanisms of damage detection and DNA repair can be deciphered. In the future, the irradiations should also be carried out in 3D cell cultures and model tissues in order to improve risk assessments for whole organisms and for humans in combination with findings from other fields such as system biology and epidemiology.

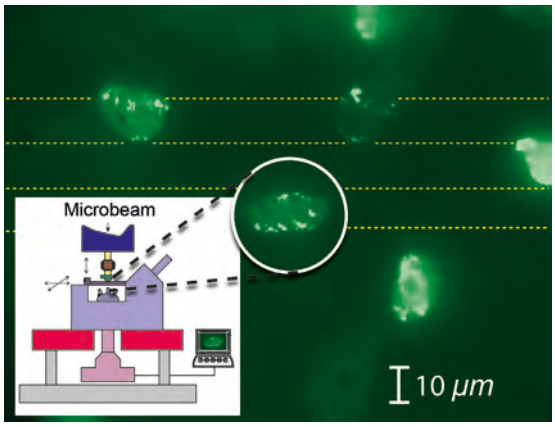

Figure 5: At the microbeam, human cells were irradiated with alpha particles in a pattern of lines with a spacing of 10 µm and approx. 1 µm between alpha particle hits (symbolized by the yellow dots). Along the particle track, double-strand breaks of the DNA occur. In the figure, they appear as bright foci, because fluorescence-marked repair proteins accumulate at the damage spots. (Photo: PTB)

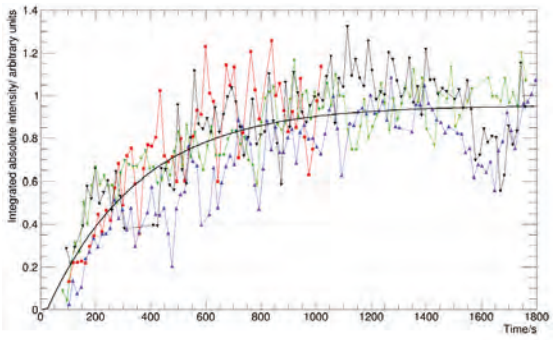

Figure 6: Kinetics of the accumulation of fluorescence-marked proteins (MDC1) at radiation-induced double-strand breaks. What is shown is the increase in fluorescence at the DSBs, in 4 different cells within a period of half an hour after the irradiation.

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