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C. R. Physique 5 (2004) 921–931
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Fundamental metrology/Métrologie fondamentale

Medicine and ionizing radiation: metrology requirements

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Available online 5 November 2004

Presented by Guy Laval

Abstract

The use of Ionizing Radiation in Medicine emphasizes the importance of Metrology for the study of biological phenomena and the development of high standard examination or treatment techniques. In particular, Radiotherapy, an important tool for cancer cure, requires the highest level of accuracy to optimize the absorbed doses delivered to the tumour and the surrounding normal tissues. The recommended upper value for the combined standard uncertainty on absorbed dose is 3.5%, lying close to or just beyond the present possibilities of radiation dosimetry and treatment delivery. It should act as a stimulus for improving the techniques and equipment from the Standards Laboratories to the clinical environment. ***To cite this article: J. Chavaudra et al., C. R. Physique 5 (2004).***

Résumé

Rayonnements ionisants et medecine : besoins metrologiques. L'utilisation des Rayonnements Ionisants en Médecine souligne l'importance de la Métrologie pour l'étude des phénomènes biologiques et la mise en œuvre d'examens ou de techniques de traitement élaborés. En particulier, la Radiothérapie, contribuant largement à la guérison des cancers, exige le plus haut niveau d'exactitude pour optimiser la dose absorbée délivrée aux tissus tumoraux et aux tissus sains environnants. La valeur maximale recommandée pour l'incertitude type combinée dans la détermination de la dose absorbée est de 3,5 %, à la limite des possibilités actuelles de la dosimétrie et des modalités de traitement. Une amélioration des techniques et des appareillages, des Laboratoires Primaires au milieu hospitalier est donc indispensable. ***Pour citer cet article : J. Chavaudra et al., C. R. Physique 5 (2004).***

Keywords: Ionizing Radiation; Radiation Therapy; Dosimetry; Accuracy

Mots-clés : Rayonnements Ionisants ; Radiothérapie ; Dosimétrie ; Précision

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1631-0705/$ – see front matter
doi:10.1016/j.crhy.2004.09.004

1. Introduction

For a long time, biological phenomena and medical activities have been considered as hardly appraisable quantitatively and thus, not very open to scientific investigation. To-day, radiation metrology is one of the major tools needed to investigate the mechanisms of action of radiations on living organisms and to develop all actions and strategies intended to protect human beings and the environment. The magnitude of radiation exposure directly influences the biological effects. Therefore, radiation metrology had to be developed to support the different types of applications especially in biology and medicine, for diagnostic and therapeutic purposes. Radiation quality, i.e., the nature of the particles and their energy spectrum, also influences the radiation effects and therefore also needs to be accurately determined.

Among the applications, radiation therapy requires the highest level of accuracy, compared to diagnostic radiology and radiation protection. This article focuses on external beam therapy for cancer treatment where particularly high physical accuracy is needed.

2. Radiobiological and clinical aspects

2.1. From energy deposition to biological effects: the quantity Absorbed Dose

The biological effects induced in the irradiated medium (tissues) by ionizing radiation are the end result of a long series of phenomena. The initial events are ionizations and excitations of atoms and molecules along the tracks of the ionizing particles. These physical perturbations lead to physico-chemical reactions, chemical reactions and finally biological effects. At each of these steps, energy is transferred, exchanged or absorbed. Therefore, the energy locally absorbed is currently taken as the measure of the magnitude of the exposure to ionizing radiation.

Absorbed dose is a rigorously well defined quantity which is used for the quantification of exposure of any type of material, including biological objects and humans to ionizing radiation. The concept and quantity 'absorbed dose' have been introduced by the ICRU [1]. Absorbed dose (expectation value of the energy imparted to matter per unit mass at a point in a medium) is a fundamental physical quantity which can be used in the different fields where ionizing radiation is used. Thus, the concept of absorbed dose has broad applications and is indeed recognized as the basic quantity in radiation therapy, radiation protection and radiobiology.

Although the biological effect is directly dependent on the absorbed dose, absorbed dose alone cannot (usually) predict the biological effect. The relationship between absorbed dose and biological effect is not unique and other factors have to be taken into account, such as: radiation quality, temporal distribution of the irradiation ('time factor'), biological effect, and more generally the conditions of the irradiation. 'Weighting functions' (or factors) thus need to be introduced to link absorbed dose to the biological effects [2].

2.2. From absorbed dose to Linear Energy Transfer (LET) and microdosimetry

At an equal level of absorbed dose, different radiation qualities may produce different biological effects. These differences in the biological effects are related to differences of energy distribution at the 'microscopic level' (or at the level of the particle tracks). So, if absorbed dose represents the energy imparted per unit mass at a point of the medium, on a very small scale of the order of the μm, the absorbed energy is not distributed in a uniform way because it is localized close to the tracks of the ionizing particles [3] and the transfer of energy takes place in a discontinuous manner in discrete amounts, resulting from the random collisions between the ionizing particles and the electrons of the medium. Absorbed dose does not express these characteristics as it is a non-stochastic quantity. It gives a global value determined in a mass of matter sufficiently large so that the statistical fluctuation is insignificant.

The biological effects result from the absorption of energy by cellular structures of small dimensions for which the non-uniform and discontinuous absorption of energy is important. When specifying an irradiation, it is thus necessary to add – to the indication of absorbed dose – an indication of the microscopic distribution of the ionizations and/or absorbed energy. This issue can be approached using two modes of representation: linear energy transfer (LET) and microdosimetry.

The LET at a point on the track of an ionizing particle represents the energy absorbed by the medium per unit length of track: it is usually expressed in keV μm^{-1}. The radiation at a point in the medium is composed of particles with various energies (and sometimes different natures), for which the LET has different values. A mean value of LET can be obtained, which is sufficient for a schematic classification of the different types of radiations, but which may conceal important differences in the distribution of LET.

LET cannot be measured, but only calculated. This requires an accurate determination of the spectrum of the particles which is usually difficult to establish. In addition, LET represents a non-stochastic quantity which does not take into account the

discontinuous character of energy transfer. To overcome the inadequacies of LET, another approach was introduced by Rossi, *microdosimetry* [4].

Microdosimetry is based on the principle that the biological effect is connected with the amount of energy imparted to a biological elementary structure of small size. The crossing of a particle ('event') results in imparting an energy, ε, to this small volume. The energy ε is a stochastic quantity and has different values from one event to another one. The distribution of the events as a function of ε provides a representation of the physical effect at a point in the medium, taking into account all the random phenomena which result from the energy transfer at a point.

The quantity ε can be measured in a small cavity filled with a gas of the same atomic composition as the biological medium, but of greatly reduced density. The cavity functions as a proportional counter. Irradiation is performed at low dose rate in order to separate the individual events and ε can be measured for a large number of individual events. The value of ε depends on the reference volume of the counter which has been selected based e.g. on the dimensions of a nucleus, chromosome, gene, i.e., a µm, tenths of µm, or a few nm, respectively.

Instead of ε, reporting the quantity 'lineal energy', $y = \varepsilon/d$ has been proposed by Rossi ($d =$ the mean chord length). The distribution of y changes only slowly with the variation of d. A comparison of the y spectra for ^{60}Co and for fast neutron beams that have been used in radiation therapy shows large differences, which explains the differences in the biological effects and relative biological efficiency values ranging from 3 to 5 for different effects relevant in radiation therapy and observed with the same absorbed dose [2] and [5].

2.3. Accuracy required in radiation therapy

The outcome of radiation therapy (local control and complications) is closely related to the dose delivered to the target volume(s) and the surrounding normal tissues ('organs at risk', OARs). On the other hand, the required level of accuracy in dose delivery in radiation therapy depends on the dose increment that can be detected clinically. More than 30 years ago, Wambersie et al. [6] and Herring and Compton [7] reported that changes in dose of 10% either way can significantly change the probability of tumour control and/or normal tissue complication. They therefore concluded that the uncertainty associated with dose should be less than ±5%. Similarly, the ICRU [8] made the following recommendation: "*the available evidence for certain types of tumor points to the need for an accuracy of* ±5% *in the delivery of an absorbed dose to a target volume if the eradication of the primary tumor is sought*". Since then, more evidence has been accumulated, supporting this recommendation.

2.3.1. Dose-effect curves for local tumour control

The dose-effect curves for local tumour control, as well as for normal tissue reaction, exhibit an 'S' shape with the steepest gradient around the 50% level of effect (Fig. 1). The relative gradient is expressed as $\Delta_{75/50}$, i.e., the relative increase in

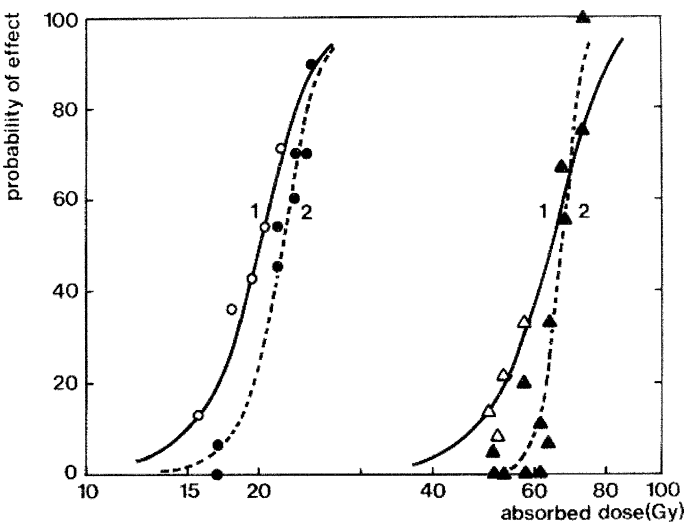

Fig. 1. Dose-effect relationships for local tumour control and for skin and intestinal damage (1-open symbols and 2-closed symbols, respectively). Randomized clinical trial comparing neutron (circles, left) and photon (triangles, right) irradiation for T_{4B} bladder tumours. All dose–effect relations exhibit a 'S' shape and a very steep slope around the 40–60% level of effect. The curves for skin and intestinal are almost identical and just one curve is shown [3].

Table 1
Relative gradient of the dose-effect curve for tumour local control

Site and size of tumour[a]	$\Delta_{75/50}$ (%)
Supraglottic larynx T2 and T3 (Shukovsky)	5
Larynx T3 (Stewart)	6
Supraglottic larynx all stages (Hjelm–Hansen)	11
Larynx all stages (Dutreix)	12
Bladder T4B (Battermann)	13
Epidermoid carcinoma head and neck (Cohen)	13
Supraglottic larynx T1 and T2 (Ghossein)	13
Skin and lip (Strandqvist)	17
Supraglottic larynx T2 and T3, revised analysis of Shukovsky data (Thames)	17
Nasopharynx T1 and T2 (Goitein)	17
Nasopharynx (Moench)	19
Lymphoma (Fuks)	21
Retromolar trigone/anterior faucial pillar T1 and T2 (Thames)	21
Bladder all stages (Holthusen)	26
Base of tongue T1 and T2 (Thames)	31
Tonsillar fossa T3 and T4 (Thames)	32
Hodgkin (Kaplan)	46
Base of tongue, T3 and T4 (Thames)	50

[a] Reviewed by Mijnheer et al. [9].

Table 2
Relative gradient of the dose-effect curve for normal tissue reaction

Tissue and type of reaction[a]	$\Delta_{50/25}$ (%)
Major chronic complications of the larynx (Harwood)	2
Peripheral neuropathy (Stoll)	3
Late skin damage (Battermann)	4
Late intestinal damage (Battermann)	4
Brachial plexus (Svensson)	5
Radiation pneumonitis (Van Dyk)	6
Skin reaction (Turesson)	7
Major complications of the intestine and bladder (Morrison)	9
Skin and lip (Strandquist)	10
Myelitis (Phillips)	15
Major and non-major complications of the larynx (Ghossein)	17

[a] Reviewed by Mijnheer et al. [9].

absorbed dose (in %) producing a change in tumour control probability from 50 to 75 %. The available data concerning the relative gradients of the dose–effect curves for several types of tumours are given in Table 1.

2.3.2. Dose-effect curve for normal tissue reactions

For normal tissue reactions, the relative gradient is expressed as $\Delta_{50/25}$, i.e., the relative increase in absorbed dose (in %) producing a change in the probability for normal tissue reaction from 25 to 50%. The available data are presented in Table 2.

2.4. Conclusion

There is an increasing amount of evidence indicating that a high degree of accuracy in dose delivery is essential for the success of radiation therapy. Accuracy requirements can be derived from the steepness – and the separation – of the dose-effect curves for local tumour control and normal tissue complications.

For a large number of tumours, the relative gradient of the dose-effect curve, $\Delta_{75/50}$, shows ranges between 10 and 20%. For normal tissue complications, $\Delta_{50/25}$ is even steeper and ranges between 4 and 10%. Radiobiological data and cellular models are consistent with these estimations.

A standard accuracy requirement of 3.5% can thus be recommended for combined type A and type B standard uncertainties [10]. This applies to absorbed dose at the specification point [11]. This required level of accuracy lies close to – or just beyond – the present possibilities of radiation dosimetry and treatment delivery: it might act as a stimulus for improving the techniques.

3. Tools for absorbed dose metrology

As the media of interest for absorbed dose metrology are primarily biological tissues, and as the field of application of dosimetry that requires the highest accuracy is radiotherapy, and to a lesser extent radiation protection, the standards developed by metrology laboratories are related to dosimetric quantities defined for media of low atomic numbers, such as air (air kerma), graphite (absorbed dose to graphite) and mostly water (absorbed dose to water) [12]. In fact, the reference quantity chosen by medical physicists to characterize radiotherapy beams is absorbed dose to water.

Evaluating a dosimetric quantity at a given point, for a given material, in the absence of any detector, requires two steps:

The first step requires the detection of a signal which is proportional to the energy imparted by ionising radiation to the sensitive volume of the detector. This implies that the relation between this imparted energy and the quantity actually measured, such as an electrical charge, a number of chemical species created under irradiation, or a temperature increase, be well known.

The second step consists in deriving from this measured quantity the dosimetric quantity to be determined. Several major problems then arise: the measured quantity is given for a finite volume and not at a point; the sensitive medium differs, in most cases, from the medium of interest; all the other components of the detector, such as external walls, perturb the field of ionizing radiation impinging the sensitive volume. All these effects must be corrected for, using experimental procedures or calculation. These corrections are minimized when the sensitive volume and the other components of the detector are composed of materials of atomic numbers close to the one of the medium of interest.

In addition, the dosimeters used for metrology must meet severe requirements in terms of repeatability, fidelity, linearity ...

Three major measurement techniques have then emerged in absorbed dose metrology: calorimetry, ionization dosimetry and chemical dosimetry with Fricke solution. The main characteristics of these techniques are described below. An exhaustive review of these techniques can be found in ICRU Report n° 64 [13].

3.1. Calorimetry

Nowadays, two types of calorimeters are used by national standards laboratories as absorbed dose standards, solid graphite calorimeters and liquid water calorimeters, which were developed more recently.

3.1.1. Graphite calorimeters

The calorimetry technique consists in measuring E, the mean energy imparted by ionizing radiation and converted into heat Q, in a thermally isolated element of known mass m (Fig. 2). The mean absorbed dose $\overline{D}$ in the core of mass m of the calorimeter is given by the ratio Q/m divided by the thermal yield r_{th}. This thermal yield is the ratio of the heat resulting from the conversion of the energy imparted to matter, to this imparted energy. Indeed, part of the energy can be expended in atom displacements and radiochemical reactions, resulting either in the absorption (endothermic reactions) or even production (exothermic reactions) of energy. The thermal yield is specific to a material and to a radiation (nature and energy).

Up to now there is no experimental evidence of a significant heat defect in graphite for the radiation considered in radiotherapy (photons and electrons of energy less than 30 MeV). The thermal yield is taken equal as one, with an associated uncertainty of the order of 0.1%. The major interest of this method lies in the straightforward relation between the measured quantity and the absorbed dose, giving a direct access to the quantity of interest.

A thermistor embedded in the core is used as the probe owing to its high sensitivity and low mass. The variation of resistance of this thermistor is measured using a Wheatstone bridge.

The electrical calibration of the system avoids requiring the knowledge of the specific heat of the core and of the thermistor sensitivity. A known quantity of heat Q_{el} is produced by electrically heating the core, resulting in a reading L_{el} of the thermistor.

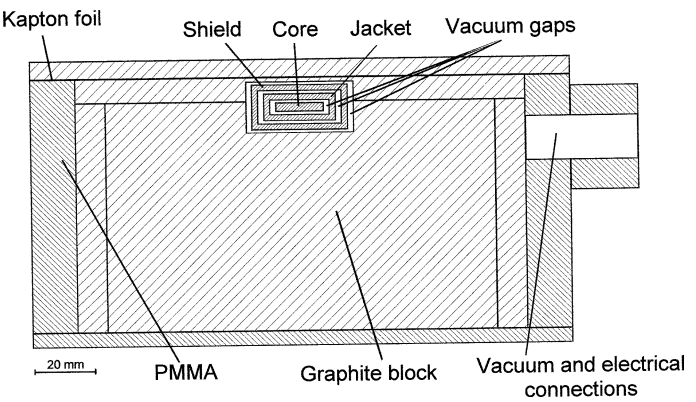

Fig. 2. Scheme of a graphite calorimeter.

The calibration factor F is the quotient of the two quantities, $Q_{\mathrm{el}}/L_{\mathrm{el}}$. If thermal conditions during electrical calibration and radiation measurement are similar, the mean absorbed dose in the core is given by the following equation for any reading L of the thermistor:

$$\overline{D} = \frac{F \times L}{m} \times \frac{1}{r_{\mathrm{th}}}. \tag{1}$$

The reference absorbed dose D in a homogeneous phantom at the point corresponding to the centre of the core can be determined from Eq. (1). Correction factors have to be applied for vacuum gaps that thermally isolate the different elements of the calorimeters, impurities, thermal yield, calorimeter–phantom density difference, dose gradients in the core, etc.

The sensitivity of the graphite calorimeter is low, about 1.4 mK/Gy. Typical dose rates in radiotherapy ^{60}Co beams are about 0.5 to 1 Gy/min and between 2 and 4 Gy/min for accelerator beams, which lead to temperature increase rates of 1 to 6 mK/min. The temperature drift of the core before and after irradiation, however, has to be stable within a few μK/min. This requires the use of specific thermal regulation processes. In spite of this, very good repeatability and reproducibility can be obtained, less than 0.1% for cobalt-60 as well as for X-ray beams from medical type accelerators. Typically, the combined standard uncertainty of the graphite absorbed dose standards can be less than 0.3% for ^{60}Co and high energy X-ray.

To obtain the quantity of interest, absorbed dose to water, a further step is necessary. Several methods can be used. The first one is to use transfer instruments that are calibrated in terms of absorbed dose to graphite in the graphite phantom in which they are placed at the reference point. These instruments are then placed at the reference point in a water phantom to characterize the same radiation beam in terms of absorbed dose to water. This necessitates the introduction of correction factors to take account of the changes of medium (water instead of graphite). This transfer can also be done by calculation.

The combined standard uncertainties of the absorbed dose to water standards derived from graphite calorimeter standards are typically of 0.4% and 0.5% to 0.6% for ^{60}Co and high energy X-ray, respectively.

3.1.2. Water calorimeters

The interest in developing water calorimetry is to obtain the quantity absorbed dose to water with the most direct method possible.

As for graphite calorimeters, the measurement is based on the increase in temperature indicated by the variation of resistance of a thermistor through a Wheatstone bridge. This thermistor is placed in a small sealed vessel, suspended in a large water phantom. The thermistor is isolated from the water in the vessel, for example in inserting it in a very thin capillary glass tube. This sealed vessel, generally made of glass, has several functions: it minimizes convection of water between the irradiated volume whose temperature increases and the non-irradiated volume. Secondly, it permits the easier use and control of the water whose high purity is required for this technique, in a smaller quantity than in the full phantom. The challenge of this technique is to determine a local change in temperature, which must be representative of the local absorbed dose. Any movement of water can bias this measurement. Therefore, most calorimeters are now operated at 4 °C, temperature corresponding to a minimum of the dilatation coefficient of water, so that any small change in temperature does not cause any change in density and thus no buoyant force and no convection. High-purity water is needed to control the heat defect of water, which can reach some percent. Indeed, ionizing radiation generates reactions of radiolysis resulting in a heat defect which is highly sensitive to impurities, including organic compounds and dissolved gases, such as oxygen. The complete understanding and precise determination of this heat defect value has, for a long time, been one of the main challenges for improving the accuracy of this technique and for confirming its ability to become a competitive primary measurement technique. At present, most laboratories developing

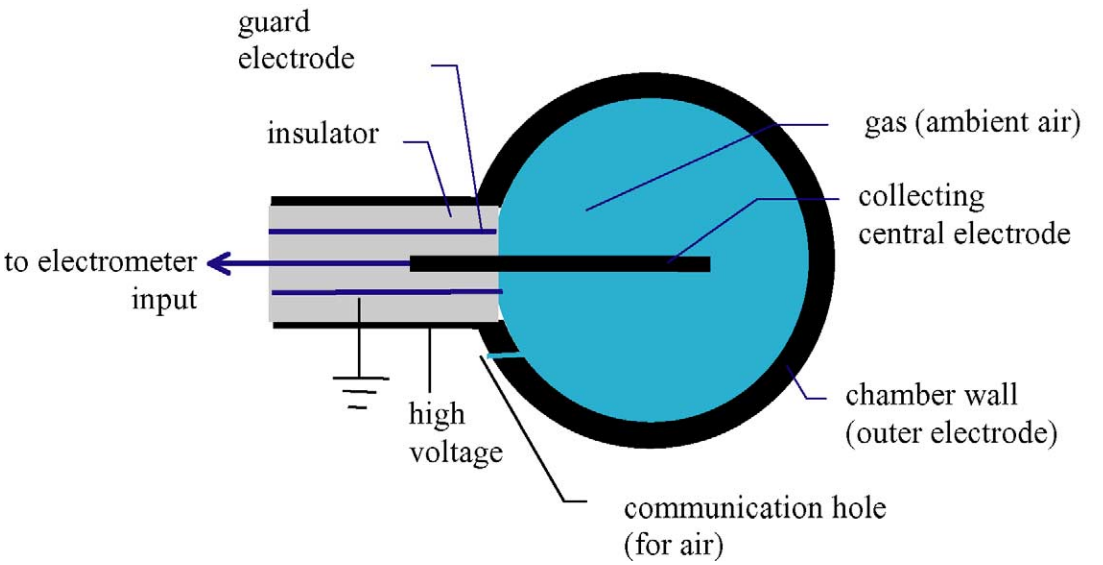

Fig. 3. Simplified scheme of an air-filled cavity ionization chamber.

these calorimeters saturate the water present in the vessel with hydrogen, nitrogen argon or a mixture of hydrogen and oxygen to obtain a stable and/or negligible heat defect. The sensitivity of the water calorimeter is still lower than that of graphite calorimeters, 0.24 mK/Gy.

In conclusion, water calorimeters are promising primary instruments, but improvements can still be made, especially in the repeatability and reproducibility of the measurements, for which results are not as good as for graphite calorimeters, and in the determination and control of heat defect.

3.2. Ionization dosimetry

Ionization has, for a long time, been the predominant technique used in dosimetry, for applications such as radiotherapy and radiation protection, and for the metrology of ionizing radiation. This can be explained by the high sensitivity and precision of this technique, properties which were pointed out very early, very soon after the historical discoveries of radioactivity and X rays. This dosimetry is based on the measurement of the electrical charge or current generated by the ionization of a gas under irradiation in a volume to which an electrical field is applied (Fig. 3). The corresponding instruments are called ionization chambers. The detection gas used for photon and electron beams is, in most cases, air in an unsealed volume, i.e. under atmospheric conditions. Since dosimetric quantities are related to the mass in which the energy is imparted, the signal generated under experimental conditions is corrected for pressure, temperature and relative humidity to obtain the signal that would be obtained under reference conditions. This requires a simultaneous measurement of these parameters at the vicinity of the detector. To deduce the energy imparted to air from the electrical charge, a physical parameter must be precisely known. This is defined as the mean energy expended in air per ion pair formed, noted W, which is assumed to be constant over the range of energies covered for the considered applications, in spite of a lack of experimental support. To make an absolute measurement with an ionization chamber, the mass and consequently the volume of charge collection must be determined by mechanical means. The ionization currents usually range between 10^{-15} to 10^{-9} A and require a good expertise in the technique of low-current measurements. In addition, corrections must be applied for the imperfect collection of the generated charges due to recombination and polarization effects.

The absorbed dose in the air of the cavity is then given by the relation

$$D_{air} = \frac{Q}{m}.\frac{W}{e}.\Pi k_i, \tag{2}$$

where Q is the collected charge, corrected for pressure, temperature and relative humidity, m the mass of gas and k_i the correction factors.

There are two types of standard ionization chambers used for metrology. Free air ionization chambers are used as air kerma standards for low and medium energy X rays for which the charge particle equilibrium can be obtained within some centimetres of air. In this case, the sensitive volume is just defined by the collimator that limits the irradiation entering the instrument and

the effective area of the electrodes that generate a parallel electrical field. Cavity ionization chambers are used as air kerma standards for cobalt-60 beams. Their sensitive volume is surrounded by an external wall, generally made of graphite, which serves as an electrode and as a medium in which charged particle equilibrium is realized.

Cavity ionization chambers of small volume (less than 1 cm^3) are used as transfer instruments in standards laboratories to derive absorbed dose to water from absorbed dose to graphite. These are also the main instruments used by medical physicists to calibrate radiotherapy beams.

3.3. Other dosimeters

Chemical dosimeters present a special interest because they can be made of aqueous solutions, very close to biological tissues (atomic composition and density). Their principle is that, in an irradiated medium, initial atomic and molecular ionizations and excitations are at the origin of chemical changes which can be used for dosimetric measurements. The absorbed dose in a sample of the detector medium can then be expressed using the following relation

$$D = \frac{q(X)}{m} . \frac{1}{G(X)} . \Pi k_i , \tag{3}$$

where $q(X)$ (mol) is the quantity of species X created under irradiation, m (kg) is the sample mass, $G(X)$ (mol/J) is the radiochemical yield of the production of X, and k_i are correction factors. The most frequently used chemical dosimeter in metrology is the Fricke dosimeter. This is an aqueous solution of ferrous sulphate in which ferric ions are produced under irradiation and measured. This dosimeter is mainly used in metrology laboratories as a transfer instrument to derive absorbed dose to water from absorbed dose to graphite.

Various dosimetric systems are also used as secondary or transfer instruments for dosimetry studies or quality control in radiotherapy. Their interest lies in their composition (tissue equivalence) or the characteristics of their response (sensitivity, linearity). Such is the case of thermo-luminescent dosimeters made of lithium fluoride (powder or pellets) which are well adapted to the large dose range met in radiation protection or radiotherapy.

3.4. Monte Carlo calculations

Due to the complexity of the interactions and phenomena considered, the experimental determination of correction factors involved in the use of dosimeters such as those described is not always possible, and the interpretation of some experiments is far from being straightforward. This is the reason why Monte Carlo codes simulating interactions of radiation with matter have been used and developed since the 1980s for metrological purposes. Their use has been progressively accepted by metrologists. Nevertheless, the codes have to be applied with special care in the field of metrology, as the evaluation of type B uncertainties resulting from the models used and from the cross section databases is not obvious.

4. Practical application to external beam radiotherapy

4.1. Dosimetry required to plan and achieve treatment

4.1.1. Treatment planning

To perform a cancer treatment, a suitable high dose must be delivered to a target volume encompassing the tumour and its possible spread, while limiting as much as possible the dose delivered to healthy tissues [11]. For this, a combination of high energy photon and electron beams is currently used. Accelerated heavy particles are used for specific indications in only a few centres so far.

The optimal treatment technique is derived from 3D dose distributions (Fig. 4), computed with specific software taking into account the patient's data (external contour, internal structures, tissue composition, target volume outlines) and the beam characteristics [14,15].

4.1.2. Measurements

Neither dose calculation, nor patient treatment can be performed without dose measurements at different levels:

– *Basic beam dosimetric data:* Current radiotherapy beams are produced by linear accelerators. They require individual beam dosimetric characterisation. This implies a large amount of systematic measurements, used to produce treatment planning software input data.

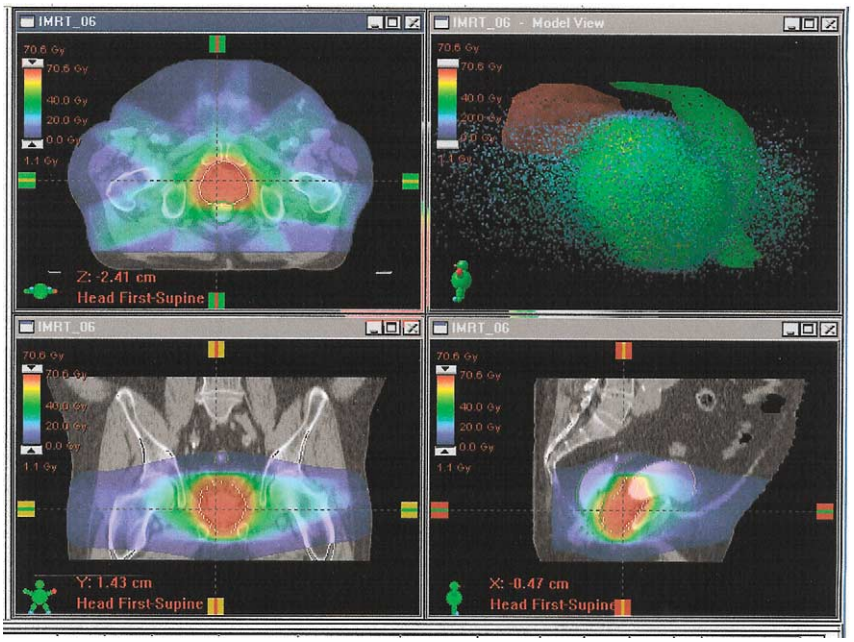

Fig. 4. Example of dose distribution planned for the treatment of a prostate cancer with external beam radiotherapy. 3D dose distributions are calculated with 3D anatomical data from CT images of a patient. To make a first evaluation of the treatment plan, 2D isodose curves (colour coding) are analysed on characteristic plans (sagittal/bottom right, frontal/bottom left, transverse/top left). A 3D display of the target volume is presented in top right image.

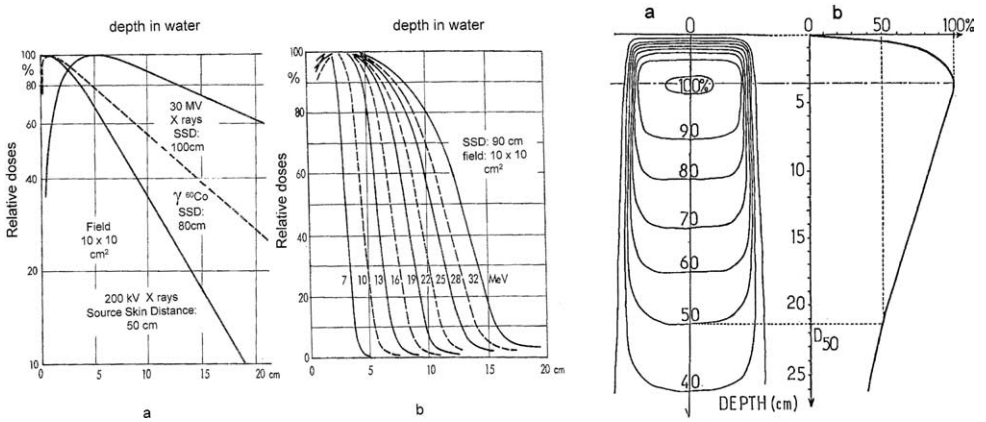

Fig. 5. Typical relative depth doses in water. Left: dose variation on the beam axis of high energy photon (a) and electron (b) beams. Obvious differences appear in the beam penetration between photons and electrons, as well as the influence of energy. Such differences are used when combining beams to optimize the treatment plan. Right: off-axis relative dose distribution in a 25 MV photon beam. The 3D dose distribution is usually represented as isodose surfaces, becoming here isodose curves when crossing a central plane containing the beam axis (a). Input data for treatment planning systems include the 'on the beam axis' depth doses (b). A central fairly homogeneous dose region is surrounded by a penumbra region, in which steep dose gradients require suitable tools for dose determination.

The dosimetric data include beam calibrations (absolute dose in Gy) at a reference point, using ionization chambers calibrated by a standards laboratory, with adequate additional correction factors, to take into account possible differences between the laboratory and the clinical beams, and requiring Dosimetry Protocols.

They also include relative measurements (dose distributions) in water phantoms simulating the patient's anatomy, on the beam axis (percentage depth doses, Fig. 5(a)) or in planes (isodose curves, Fig. 5(b)), using ionization chambers or film dosimetry with other corrections to take into account the changes in dosimeters response in the medium (use of protocols).

To determine the dose distributions in actual patients, the computer algorithms correct for the differences between the water phantom and the patient size, shape, density and atomic composition.

– *Beam monitoring*: The high level accuracy required for the dose delivered with each beam needs independent monitoring using an ionization chamber crossing the whole beam, currently calibrated daily for all possible treatment conditions. In addition, in vivo measurements are sometimes needed in selected points within the patients; they are often performed with thermo-luminescent dosimeters, or semi-conductor probes.

4.2. References dosimetry protocols for radiotherapy

References have been developed by national standards laboratories, particularly to enable medical physicists to calibrate their dosimeters used in external radiotherapy in terms of absorbed dose to water.

After the historical quantity 'exposure', the first standards developed and proposed by standards laboratories were air kerma standards in photon beams generated by X-ray generators and cobalt-60 gamma beams. These primary standards are still given with a combined standard uncertainty of 0.2 to 0.5%.

The reference instruments of medical physicists (transfer cavity ionization chambers) were then, and are still, calibrated by standards laboratories in terms of air kerma. However, the required quantity in clinical radiotherapy is absorbed dose to water for the electron and photon beams produced by linear accelerators. As a result, Dosimetry Protocols have been published in order to derive the needed calibration coefficients from those given by standards laboratories. In these protocols, different parameters are recommended for all the commercially available types of chambers and all types of radiation (photon, electrons) and beam qualities covering the range of external radiotherapy. For example, the IAEA protocol of 1987 [16] or other national protocols like the French CFMRI [17] published in the same period, were based on air kerma standards for cobalt 60. At that time, these standards for air kerma were more usual and validated at the international level, especially through BIPM comparisons, than standards for absorbed dose to water.

In the meantime, many national standards laboratories have realized absorbed dose to water standards for cobalt-60 beams and validated them through BIPM comparisons. In a few laboratories equipped with accelerators, this work was also carried out for high-energy X-ray and electron beams. This lead to the publication of new protocols based on absorbed dose to water (for example [18,19,13]). These protocols result in reduced difficulties and uncertainties for users. For a given type of chamber, only one factor corresponding to the beam quality Q of interest, named quality factor k_Q, is needed to derive the calibration coefficient $N_{D,w,Q}$ from the one given by the standard laboratory for cobalt-60, $N_{D,w,\mathrm{Co}}$.

$$N_{D,w,Q} = k_Q N_{D,w,\mathrm{Co}}. \tag{4}$$

A task of national standards laboratories is to validate or improve the accuracy of these published quality factors k_Q with a better control of uncertainties.

5. Conclusion: metrology of ionizing radiation must be improved

Meeting the accuracy required in Section 2.4 for the dose delivered to the patient for a given treatment, implies a high level of accuracy in each of the multiple steps of the whole procedure. Starting from the accurate beam calibration, uncertainties are introduced in beam data acquisition, beam monitoring and dose calculation. In addition, uncertainties due to the patient's data and uncertainties linked to the patient's set-up and the irradiation geometry at each session must also be considered (a typical treatment is made of 20 to 30 sessions). As a result, in the clinical conditions, the uncertainty on the dose may reach 2% at the reference point of a given beam, and may exceed the recommended value of 3.5% for the dose distributions.

This enforces the need for improved treatment techniques, but also for the availability of metrological references more adapted to the actual clinical conditions and expressed in quantities as close as possible to the quantities used by the medical physicists in clinical practice.

Acknowledgements

The authors thank Dr P. Allisy-Roberts for her valuable comments and suggestions.

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