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When and how can we improve precision in radiotherapy?

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Introduction

I appreciate the great honour to be asked as a Hospital Physicist to deliver this third Klaas Breur Memorial Lecture at the European Society for Therapeutic Radiology and Oncology. I feel very proud to join Bernard Pierquin and Jack Fowler in this distinguished award but it is not an easy task after their superb lectures. In particular Jack Fowler being both a radiobiologist and a physicist has already covered the whole field of physics in radiotherapy and radiodiagnosics and I was often tempted just to copy some paragraphs of his excellent lecture.

I had the chance to meet Klaas Breur several times, and I have always appreciated how open-minded he was to all the aspects of radiotherapy and radiobiology. All his work was deeply marked by the search for accuracy, and I am very glad to have the opportunity to honour his memory with such a subject.

We, who entered the field of radiotherapy in the fifties, had a great chance to live three successive revolutions. The first one, in the early fifties, was the jump from the conventional X-rays to the high energy photon beams: the first patient treated with the 20 MV photon beam of the betatron in our Institute was irradiated in October 1953. The second revolution in the mid-sixties was the introduction of computers in radiotherapy. It was rapidly followed by the third one on diagnostic imaging which would not have been feasible without computers. This tremendous advance of technology accelerates from year to year but I wonder whether I have a chance to live a fourth revolution!

The physicist facing such fantastic progress is fascinated by so many wonderful toys but he feels sometimes like a sorcerer’s apprentice wanting every day more powerful tools, but not always sure of being able to master their outcome. Rabelais who was not only a famous French writer but also a physician noted that: “Science sans conscience n’est que ruine de l’âme” (Science without conscience is nothing but the ruin of spirit).

One of the most embarrassing questions we have to face, is: are we sure that these new techniques will improve patient cure? The answer is not as obvious as it seems at first if one wants to demonstrate it scientifically. One way to approach this problem is to ask a much more modest question: could these new techniques improve accuracy in radiotherapy? Immediately followed by a further question: what is the responsibility of the physicist in improving accuracy in radiotherapy?

* Lecture held during the third ESTRO annual meeting, 12 September 1984 on the occasion of the award of the Klaas Breur gold medal.
Before answering these questions one must consider what is meant by precision in radiotherapy and how it can be expressed.

**Precision in radiotherapy**

The first publication, to my knowledge, listing the various possible errors in radiation therapy was the last chapter of the ICRU [19] report 10d on clinical dosimetry, prepared under the impulse of Maurice Tubiana and published in 1962. The last recommendation of the report is still worth considering: "Some method of immobilising the patient and of checking the patient's position during treatment should be used". Unfortunately, no great strides have been made in this direction.

Precision in radiotherapy is required at different stages. The first is the knowledge of the dose to prescribe; this is clearly the responsibility of the radiotherapist. The precise determination of the target volume to be irradiated is also the responsibility of the radiotherapist. For many years, the aim of radiotherapy was to deliver a dose as uniform as possible to the target volume and as low as possible to the healthy tissues outside this volume. In mathematical terms it means that the ideal profile of the dose distribution through the target volume is assumed to be rectangular. Such a rectangular dose distribution assumes either a rectangular distribution of the density of malignant cells throughout the target volume, or the ignorance of that distribution. The estimation of the density distribution of the malignant cells weighted by their respective radiosensitivities could be a more sensible approach; it is the common responsibility of the radiotherapist and the radiobiologist to make this estimation in the future.

The accurate localisation of the target volume is essentially a clinical task, but techniques are needed in which the physicist is necessarily involved (simulation, CT imaging, etc.). It is achieved most often by close cooperation between the radiotherapist and the physicist.

A further requirement in precision may be the estimation of the difference between the prescribed dose to a reference point in the patient (in general the tumour center), and the dose effectively delivered to that point; this is the responsibility of the physicist. Errors which can occur include the physical and geometrical parameters of the treatment as well as the determination of the absorbed dose in a phantom.

It is generally assumed that the physicist has to ensure that the dose distribution achieved is in good agreement with the intended dose distribution. Two kinds of errors which can occur are: errors linked to the calculation of the dose and those linked to the set-up of the patient for daily treatment.

Errors in the determination of dose distribution involve those in the determination of the basic data of the radiation beam, patient data and the computation programme, which are too often neglected. All these errors are the responsibility of the physicist.

The set-up of the patient can be divided into three steps: setting of the machine parameters, patient positioning and patient immobilisation during treatment.

Precision during the first step is clearly the responsibility of the physicist, but that during the two other steps is the common responsibility of radiotherapists, physicists and technicians.

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Fig. 1. Average regression of tonsil tumours for patients randomised into two groups A and B treated with dose fractions of 2.23 and 2.46 grays, respectively, 3 times a week as a function of the number of days. The difference is statistically significant although the number of patients treated is small (19 and 22 respectively).
Precision required in determining the dose delivered to the patient

Wambersie et al. [35] and Herring and Compton [16] made an estimation of the degree of precision required in the dose delivered in radiotherapy. Herring and Compton reviewed the publications that showed steep variations of biological effects of doses, either on the tumour [32,33] or on normal tissues [10,27,33]. They concluded that changes in the dose of 10% either way can significantly change the probability of either necrosis or local control, and therefore the uncertainty associated with dose distribution should be less than plus or minus 5%.

Two experiences from the Institut Gustave Roussy are worth mentioning: one was related to tumour regression and was published in 1967 [9], the other related to normal tissue reactions but has unfortunately not yet been published.

The first study, carried out in the early sixties, was intended to demonstrate that high energy photons or electrons give the same effect on tumours for the same dose. Patients with squamous cell carcinoma of the tonsil were randomised and three observers recorded the tumour regression during the treatment. To our great surprise a significant difference appeared between electron and photon treatments nominally identical in dose (18 fractions of 2.5 Gy in 40 days). A small number of patients, 20 in each arm of the trial, was enough to show a definitely smaller efficiency of the electron treatment (Fig. 1). This lead to the discontinuation of the trial. A new calibration of the dosimeter for both photons and electrons was achieved with ferrous sulphate during the following months and showed for the high energy calibration, a departure from the cobalt-60 calibration which had been used during the trial. The new calibration lead to a 7% difference between the doses of electrons and photons. This could explain the difference observed in tumour regression between the two kinds of treatment.

The second experience was described in an internal report [6] as follows:

The radiotherapist in charge of gynaecological patients treated with high energy photons (25 MV) on the Sagittaire (CGR MeV linac) mentioned to the physics department that he suspected an error in dosimetry because he observed reactions on patients which were more severe than usual. These were skin reactions on the skin folds and also diarrhoea in patients irradiated to a prescribed tumour dose equal to 5000 rad (50 Gy) on the whole pelvis 5 times a week for 5 weeks. After a careful rechecking of the linac, we found an underestimation of the calibration factors of the monitor leading to a systematic overdosage of the patients; the reason was the misuse by a junior physicist of the correction factors applied to the ionization chamber. The overdosage was estimated to be 10% between September and November 1970 and 7% between November 1970 and March 1971. The number of patients who had been overdosed for a part or for the full course of their treatment was 21 between September and November 1970 and 67 between November 1970 and March 1971. Fifty patients out of the 88 overdosed had finished their treatment course over 2 months before the radiotherapist suspected the error. No striking reaction was observed on the other (non-gynaecological) patients.

These two experiences concur with the conclusions of Herring and Compton, and emphasise the need for overall precision on the tumour dose of 5%.

Precision in delivering the dose to the prescribed target

Errors of localisation, patient set-up and dose distribution may all contribute to the underdosage of part of the target or to the overdosage of healthy tissues. They may therefore lead to a marginal recurrence or to severe reactions of critical organs respectively. The effect of these errors on the final precision is similar, but they should be clearly identified because their different origins require different solutions.

Errors in patient set-up as well as patient movements during treatment lead to a smoothing of the dose distribution in the margin of the target volume and in the vicinity of this volume. These create an enlargement of the so-called penumbra region.
To my knowledge, there are only a few clinical data leading to a statistical evaluation of the degree of precision required for the fitting of the treated volume to the target volume, and none on the dose uniformity required in the target volume.

Clinical studies generally assume that each treatment beam adequately traverses the desired target volume during every session and that the total absorbed dose at each point of the target volume is equal to the prescribed dose. One question could be asked about the dose homogeneity throughout the target volume: what should be the optimal dose distribution in the target volume for a given tumour?

It is obvious that there is no simple solution to this complex problem. The solution depends upon the clinical and biological characteristics of the treated tumour: the magnitude of the absorbed dose to be delivered, the size of the target volume, the malignant-cell density distribution, the relative radiosensitivity of the cells in the various parts of the target volume, the proximity of critical organs, etc. The variety of choice for the best solution regarding dose-uniformity is illustrated by the two following examples.

Firstly, intracavitary treatment of cervical cancer implies a much higher dose to the central part of the target volume than to its border. This large dose variation is not only tolerated but is considered as the most important feature of brachytherapy. The dose to be delivered to the tumour is in fact limited by the maximum dose which can be tolerated by the organs at risk.

Secondly, the local overdosage of the central part of the tumour at the end of the treatment, known as boost, deliberately intends to deliver a higher dose to the most resistant part of the tumour.

The accurate determination of the non-uniform dose distributions, whether intended or not, is essential for the correlation between the doses and the clinical observations. It is the only way to help the clinician to draw a final judgement on the uniformity required.

**Different kinds of error**

*From random and systematic errors to mistakes*

It is remarkable that the assignment of an uncertainty* to a published numerical value is a rather new practice even in fundamental sciences. Probability calculations were first performed by Pascal** in the middle of the seventeenth century. He established the basis of statistics in a private correspondence with Fermat**, a detailed analysis of the theory was published 2 years later, with substantial additions by Huygens [18]. The theory of errors was fully developed during the nineteenth century. However, probabilities were only applied systematically for uncertainty estimation during the last 50 years. Before that time no explicit mention of the precision was ever made in a scientific publication, even under the signature of the most famous scientists. A scientist based his judgement of the reliability of published results upon his knowledge of the personality of the author, simply because he might know personally most of the people working in his field, as was pointed out by Müller [25]. The rapid increase in the number of scientists has led to the reputation of the scientist being replaced by an objective evaluation of the precision.

In the field of assessing uncertainty, medicine and radiotherapy appear to be in the position that fundamental sciences were in 50 years ago. An estimated uncertainty is rarely associated to the dose delivered to patients. In spite of the large use of statistics for the estimation of the results of a treatment, such as cure-rate, number of recurrences, etc., the absorbed dose to the tumour is always assumed to be known exactly. It is clear that the re-

* As recommended by the “Bureau International des Poids et Mesures” (BIPM, [4]), the words “uncertainty” and “error” will be considered as synonyms. So it is, with “precision” and “accuracy”.

** Blaise Pascal (1623–1662) and Pierre de Fermat (1601–1665), French mathematicians.
liability of any published dose-effect relationship depends upon the prestige of the Institute of origin if not specifically upon the reputation of the radiotherapist.

Radiotherapists have many excuses or good reasons for not admitting uncertainties. First the clear statement of an uncertainty raises psychological and legal difficulties. Non-radiotherapist clinicians as well as patients themselves need to be reassured: they believe in magic numbers. They would probably not tolerate the acknowledgment of an accepted error. Furthermore, one suspects that the radiotherapists would be inclined to understate the errors because of the fear of legal suits. Another excuse is probably more relevant in that it is mainly the responsibility of the physicist to estimate errors.

Two kinds of errors are usually considered, random and systematic errors. Random errors can be derived from repeated measurements or repeated adjustments of a given parameter in the same conditions: they can be expressed in terms of a standard deviation for statistical considerations.

Systematic errors are introduced by a poor measurement process, a poor initial adjustment, the deviation with time of a parameter or an incorrect procedure. Systematic errors are unknown by nature. It is hoped that when a systematic error is identified, it can be immediately eliminated. However, this is not possible for systematic errors in fundamental physical constants. Possible systematic errors are sometimes expressed in terms of their suspected upper limit and may lead to an overestimation of the total uncertainty.

Both a random error and a systematic error can be associated to each parameter. For instance, the distance from the source to the patient skin is adjusted every day by the technician with a given random error due to the reading of the SSD-indicator and to the unavoidable movements of the patient (such as breathing). If the SSD-indicator is not correctly calibrated, a systematic error is included, which can be much larger than the random error and leads to a constant error on dose for every patient treated with this facility. However, this systematic error has to be considered as a random error in an intercomparison between different radiotherapy centers*

Systematic errors are obviously related to quality assurance programmes of the therapy centre in which the treatments are achieved. They may vary considerably between centers, depending on the number and the experience of the staff. In a top-level centre, systematic errors should be quite negligible in comparison to random errors. In a small centre, systematic errors may be much larger than random errors. Obviously it is much better to spend time correcting errors rather than estimating them. A systematic error which is identified but not corrected becomes a mistake.

Human mistakes caused by inattention, misunderstanding or misjudgement are not considered here. In principle, they should be completely eliminated by a proper system of checks and cross-checks of human performance. However, in practice the cost of such checks would be very high.

The total uncertainty may be estimated by combining the various uncertainties in quadrature. For instance, assuming that 10 parameters introduce small uncertainties equal to 0.2% and that one parameter introduces a large uncertainty of 2%, the cumulated uncertainty is equal to 2.1% in which the contribution of the 10 small uncertainties is quite negligible. The weakest point of the chain is obviously responsible for the total uncertainty. Every possible effort should therefore be made to reduce the largest uncertainties.

For many years, scientists combined errors using complex rules which differed from one centre to another. The most common method was to add linearly the systematic errors and to combine in quadrature the random errors. Such a procedure led to an estimated maximum error, assuming that the errors are always additive. This maximum error was generally far from realistic. The Bureau International des Poids et Mesures [4] recently recommended combining uncertainties, whether random or systematic, in quadrature to obtain the overall uncertainty.

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* This is one of the reasons why BIPM [4] has suggested replacing the words “random” and “systematic uncertainties” by “category A” and “category B uncertainties”.
uncertainty. This overall uncertainty could be multiplied by a constant factor which is defined by the experimenter according to the type of application. Its numerical value should vary between 1 and 3 and be clearly stated.

**Evaluation of the overall uncertainty**

Errors at various stages of radiotherapy may be evaluated in two ways: evaluation a priori following theoretical considerations together with the judgement of experienced physicists, and evaluation based on large intercomparisons.

*Evaluation a priori of the errors* has been made by Loevinger and Loftus [24] in two extreme situations, a top-level radiotherapy centre (optimal model) and a small centre (minimal model). Johansson [2] considered an optimal model in which systematic errors in a given quantity are always small or even negligible compared with random errors, when the two categories of errors are present.

*Evaluation based on large intercomparisons* between radiotherapy centres were performed by Shalek et al. [31], Gagnon et al. [13], Samulski et al. [30] and Johansson [21]. They measured the error distribution for some important parameters and calculated the standard deviation. This is certainly the most sensible way to estimate the state of the art in a given country and to determine the weakest point in the chain. Unfortunately the last steps, including determination of patient data and patient setting-up, are not included in these intercomparisons. The adequacy of treatment portals to target volume at the time of simulation and treatment planning [23] or during the course of treatment was not regularly checked.

The final judgement on the total uncertainty in radiotherapy is derived from the statistical comparison of clinical results from radiotherapy centres using similar radiotherapy protocols for a selected disease; Gagnon et al. [13] and Kinzie et al. [23] have shown the importance of such well-documented studies.

**Sources of error in radiotherapy**

The sources of error in radiotherapy which are the responsibility of the physicist can be divided into six different sections:

1. The treatment unit parameters;
2. the measurement of the absorbed dose at a reference point in a phantom;
3. the measurement of the dose distribution;
4. the patient’s data;
5. the treatment planning;
6. the set-up of the patient.

When analysing the relative importance of uncertainties in each section, the physicist should consider whether the related error leads either to an error in the dose delivered to the patient or to an error in the dose distribution, or possibly both. For instance, a systematic error of $-5\text{ mm}$ on the collimator setting leads to a minor error ($0.5$ to $2\%$) on the dose delivered to the tumour and also leads to a systematic underdosage of the $5\text{ mm}$ margin of the target volume: the narrower the penumbra, the higher the underdosage.

**The treatment unit parameters**

These are the optical, digital or mechanical devices: i.e., SSD-indicator, pin-and-arc devices, head-rotation indicator, light localizer and collimator-size indicator. Indications of the treatment-couch position should be included among these parameters when they are used to position the patient, for example, in isocentric techniques.

Random errors on these parameters have to be considered during three different steps:

- the absorbed dose measurement at the reference point in reference conditions;
- the variation of the absorbed dose at the reference point in relation to those parameters;
- and also the day-after-day adjustment of the parameters for patient treatment. Therefore, they have to be included three times in the calculation of the overall uncertainty.
On the other hand, systematic errors on these parameters should be included only once in the overall uncertainty because they are constant for a given treatment unit during the full treatment process. The magnitude of the random uncertainties in the setting of the treatment-unit parameters depends on the ability of the technicians to adjust the various parameters and should be estimated in each radiotherapy department. The magnitude of the systematic uncertainties depends on the quality-assurance programme in use. The highest permissible limits of systematic uncertainties should be recommended and ensured by appropriate checks of each item described in the quality-assurance programme.

Table I shows uncertainties in some typical parameters which were estimated by various authors: Johansson has estimated the random uncertainty in the parameters adjusted by physicists for the measurement of the absorbed dose at a reference point. Gagnon and Samulski have stated criteria and have determined the percentage of centres inside or outside each criterion. The large number of centres which are outside the criterion (39, 12 and 24%) for the first three parameters of Table I shows that the uncertainties estimated by Johansson are not realistic. These data show that the systematic uncertainties, probably related to inadequate quality-assurance programmes, are rather large. The last column of Table I shows the criteria used in the quality-assurance programme of the Institut Gustave Roussy. These parameters are checked systematically every month and the indicators are readjusted when the estimated error is equal to or larger than the accepted criterion.

A check and control system reduces the random errors to very small values and eliminates mistakes. However, it will not reduce the systematic errors detected by Gagnon and Samulski, and will lead to underestimation of the risk of errors if it is not associated with a high precision quality-assurance programme. Bentley [3] reviewed three studies [12,22,28] on the subject of monitoring the set-up parameters of high energy radiotherapy machines and the measurement of the rate of mistakes. The amount of mistakes among the thousands of set-ups in the three centres is roughly the same. The error rate varies between 0.1 and 0.9% depending upon the particular parameter checked and also the magnitude of error that is considered to be a mistake. As a mistake made in one treatment fraction is generally rectified in the next, it therefore has a negligible effect on the whole course of treatment. This low rate of mistakes is worth considering in an evaluation of a cost-benefit ratio.

**The measurement of the absorbed dose at a reference point in a phantom**

The magnitude of the random uncertainties in the absorbed dose determination depends mainly on

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<tbody>
<tr>
<td>SSD indicator</td>
<td>1 mm</td>
<td>–</td>
<td>2 mm*</td>
<td>2 mm</td>
</tr>
<tr>
<td>Light and radiation field coincidence</td>
<td>1 mm</td>
<td>3 mm</td>
<td>3 mm</td>
<td>1-3 mm*</td>
</tr>
<tr>
<td>Light field size and indicator agreement</td>
<td>–</td>
<td>–</td>
<td>2 mm</td>
<td>1-3 mm*</td>
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<tr>
<td>Arm rotation indicator</td>
<td>–</td>
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<td>1°</td>
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<tr>
<td>Collimator rotation indicator</td>
<td>–</td>
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<td>1°</td>
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<tr>
<td>Couch height indicator</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2 mm</td>
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</table>

* The criterion is the uncertainty which leads to a 0.5% variation of tumour dose: it is about 2 mm for a 80 cm SSD and 2.5 mm for a 100 cm SSD.

* The criterion is 1 mm for a 5 × 5 cm field and 3 mm for a 30 × 30 cm field.
TABLE II
Overall uncertainty in the absorbed dose at the reference point.

<table>
<thead>
<tr>
<th></th>
<th>60Co (%)</th>
<th>X-rays (%)</th>
<th>Electrons (%)</th>
</tr>
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<tbody>
<tr>
<td>Shalek [31]</td>
<td>3.4</td>
<td></td>
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<tr>
<td>Loevinger and Loftus [24]</td>
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<tr>
<td>optimal</td>
<td>2.4</td>
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</tr>
<tr>
<td>minimal</td>
<td>4.4</td>
<td></td>
<td></td>
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<tr>
<td>Gagnon [13]</td>
<td>2.4*</td>
<td></td>
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<tr>
<td>Samulski [30]</td>
<td>2.7</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Johansson [21]</td>
<td>1.7</td>
<td>2.3</td>
<td>2.5</td>
</tr>
<tr>
<td>estimated</td>
<td></td>
<td></td>
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<tr>
<td>determined</td>
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</tr>
<tr>
<td>experimentally</td>
<td>1.4</td>
<td>2.8</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* In this intercomparison some chambers have been directly calibrated in a Secondary Calibration Laboratory and some have not. For the former the standard deviation is only 2% but it is as large as 4% for the others. They correspond to the optimal and minimal models of Loevinger and Loftus.

the accuracy of the various parameters used. The quality of the dosimeters and that of the radiotherapy equipment used, leads to a general agreement on the random uncertainties to be considered, provided the physicist agrees to use a well-established and well-documented protocol [1, 5, 17, 26]. The systematic uncertainties are generally small because the physicist is more naturally inclined to devote his efforts towards the more fundamental measurements. However, Johansson [21] has shown that in some centers the largest systematic uncertainties in the measurement of the absorbed dose were associated with the determination of air pressure and temperature due to the poor calibration of some of the barometers and thermometers used. Table II shows the estimated overall uncertainty in the absorbed dose at the reference point in a phantom. The uncertainty is larger for electron beams than for photon beams, mainly because of the uncertainty in the energy determination at the depth of measurement.

The measurement of the dose distribution

Two types of uncertainties have to be considered: the uncertainties in the measurement of the dose distribution and the uncertainties in the reproducibility of the dose distribution.

Errors in the dose distribution measurement include errors in the detector response, in the position of the detector and those due to the nature of the phantom. Systematic errors in the detector response are mainly due to its dependence on radiation quality and on dose-rate.

Errors in the position of the detector and those due to the nature of the phantom are usually small random errors unless a mistake was made on the corrections to be applied. These corrections were published in the various protocols.

Large systematic errors or mistakes could be made when dose distributions are not measured for the treatment unit in use. Dose distributions adopted can originate from an atlas, from literature or they are supplied by the manufacturer with the treatment unit. Lastly, they can be computed with a treatment planning console from basic data provided by the programme author for another treatment unit. These dose distributions should be checked carefully for a few representative beam configurations before being used for patient treatment planning. Depth doses are generally accurate for cobalt-60 beams but large differences are often found between linac X-ray beams of the same nominal energy. Larger differences are found in the penumbra region.

Electron beam dose distributions should, without exception, be measured for every linac because they greatly depend upon the energy adjustment of the linac and upon the mechanical and geometrical features of the collimator.

The overall uncertainty in the measured dose distribution is smaller for cobalt-60 beams than for linear accelerators, as demonstrated by Johansson [21] and it is also smaller for X-ray beams than for electron beams.

The difference between cobalt-60 γ-ray beams and X-ray beams is ever greater when the reproducibility of dose distribution is considered. Small variations in the direction of the emitted X-ray beam are amplified by the compensating filter leading to large differences in dose distribution. Beam
symmetry has to be checked at regular and frequent intervals at least for the four main beam directions because specific adjustments may be needed for each rotation angle of the linac head. Furthermore, the beam quality has to be checked carefully in the quality-assurance programme.

Even in cobalt-60 γ-ray beams, the uniformity of the dose distribution must be checked at regular intervals in order to adjust the collimating device. Johansson estimated the standard deviation on the dose at any point relative to the dose at the reference point. He only considered square and rectangular fields and estimated the uncertainties to be 2.6, 3.3 and 3.8% for cobalt-60 beams, high energy photon and electron beams, respectively.

The patient's data

Accurate treatment planning requires a knowledge of cross-sectional anatomy for three main reasons: firstly, for determination of the extent of the tumour and its localisation with respect to surrounding tissues, body outline and landmarks; secondly, for determination of the position and size of critical organs which may need to be protected; thirdly, for quantitative information on density distribution throughout the irradiated volume to enable corrections to be made for the attenuation of X-ray beams or the absorption of electron beams in different materials.

Mechanical methods using lead wires or calipers are the most frequent contouring techniques in use in radiotherapy departments. Unfortunately, they can lead to errors of several centimeters particularly in the abdomen and chest. A more sophisticated device using a sensor mechanically linked to a pen allows the precise drawing of the patient's outline to within a few millimeters. However, the determination of internal structures makes matters more complicated. Orthogonal radiographs, with lead scales to determine the magnification factor, are a great help in determining the size and location of organs, but only the projected dimensions of the anatomical structures can be determined by this method.

At the Institut Gustave Roussy the first determinations of anatomical cross-sections were performed in 1954 with conventional axial tomography on sitting patients treated with the betatron [11]. Since 1974, a Toshiba tomograph has been used on lying patients. Body outline is determined by means of a set of small lead wires placed on the skin (Fig. 2) with an uncertainty of ±2 mm. Body and organ contours are read out and digitized by means of a curve follower used as input in the computer programme. Unfortunately, only bones, lungs and a few opaque organs could be localised because of the poor contrast between the various soft tissues. Uncertainties of a few millimeters can be achieved on the lateral edge of the lung contour but they can also be as large as a few centimeters in the anterior and posterior parts of the lungs where large artifacts occur.

The recent development of CT scanners has provided good quality images of patient cross-sections. The current generation of CT scanners have spatial and contrast resolutions capable of covering the needs of radiotherapy. However, there exist certain causes of error in the determination of the dimensions of organs or target-volume and also in the determination of the densities of organs.

CT scanners are optimised for diagnostic purposes and CT scans are often obtained in the radiodiagnostic department before radiotherapy is planned. The primary problem which faces a diag-

Fig. 2. Transverse tomographs of a prostrate patient. The lead wires placed on the skin show the body contour. Two lead wires identify the table top.
nostician is whether or not disease is present and if so, what sort of disease is it. The therapist, on the other hand, is supposed to know of the tumour's existence, but he must also determine its extent in all directions, the position and size of adjacent structures and the relationship between the organs and the external landmarks which are to be used for setting-up the patient in the treatment room.

As only a small change in the position of the patient may lead to large variations in the position of organs with respect to the body outline, it is essential that the patient set-up be identical for treatment and for CT scanning (Fig. 3). The reproducibility of the patient's position can only be ensured if the radiotherapist, or a well-trained therapy technician, assists the diagnostician in positioning the patient on the CT couch. Difficulties arise from the differences between the CT scanner and the treatment units. The CT gantry tunnel is often too small in diameter and this makes it impossible to set the patient in the treatment position. The CT couch is narrower than the usual treatment couches and should be flat and without a mattress. All support devices should be reasonably radiotransparent so as not to produce artifacts.

Turning the patient back from a supine to a prone position to treat anterior and posterior fields, respectively, results in large variations in the body

![Fig. 3. CT scans of a head. The position of the patient's head for CT scans (a Reid's angle = 0) usually differs from the treatment position (b, Reid's angle = α).](image)

(c and d) Show the large differences observed in CT scans performed in positions a and b, respectively.
contour, in the relative position of different organs and even in the density of the various parts of the lung (Fig. 4). The lung density calculated from CT numbers usually varies by 30 to 50% between the lowest and the highest part of the lung whatever the patient's position: the highest part of the lung is always more transparent than the lowest part. The benefit gained in the accurate determination of the patient's data would be lost if the position of the patient was modified with changes in the beam direction.

Although the duration of the scanning cycle has been progressively reduced from about 20 min to a few seconds, thereby decreasing the effect on the image of patient motion, a whole examination with 20 adjoining sections or more lasts about half an hour and any movement of the patient will make the 3-D reconstruction of the volume very difficult. Another difficulty may arise with the patient's breathing. When the CT has a cycling time of a few seconds, it is possible to ask the patient's cooperation in holding his/her breath during the scanning. However, the duration of a radiotherapy session makes holding one's breath impossible, therefore it seems advisable to assess the motion of tissues during treatment and to average out the dimensions and densities over several respiratory cycles (Figs. 5 and 6). Large differences may be noticed between images obtained during holding one's breath and in normal breathing.

The other causes of error have been widely analysed in the literature [8]. An uncorrect choice of window level and window width may lead to large errors in the dimensions of organs when they are

Fig. 4. CT scans of a patient in supine (a and b) and prone (c and d) position. Large differences are observed in both the body contour and the organ positions for the two sections shown.

abdomen (a and c) and thorax (b and d), when the position of the patient is modified.
determined directly from the image: the automatic determination of contours with a convenient computer programme suppresses that cause of error. A poor correction of the CT numbers for tissue filtration may produce an error as large as 7–10% on the tissue density of deep organs calculated from the CT numbers: this error may be much larger than the error made when assigning average densities to organs as published in the literature; the only exception is the lung, the density of which can vary from 0.15 to 1 depending on the age of the patient and the functional status of the lung.

Several authors have underlined the great potential of CT [7,14,15,34] for improving radiation therapy through accurate localisation of tumour and critical normal structures, as well as more accurate determination of organ densities.

The recent advances in NMR imaging may certainly help to determine the extent of the tumour. However, it is not expected to replace CT imaging for treatment planning because the NMR signals are not related to tissue densities in the same way as CT numbers and therefore cannot be used directly for dose calculations.

The treatment planning

It is now common practice to use computers for treatment planning. The addition of radiation beams is a task ideally suited to computer techniques and many workers throughout the world have contributed to the analysis of the problem and have proposed numerous computation methods.

In computer calculations the random errors are reduced to a quite negligible level: the doses can be calculated with nine significant figures and the ran-

![Fig. 5. CT scans of a patient breathing normally (a and b) and holding his/her breath (c and d). Large differences are observed in both the body contour and the organ positions for the two sections shown, abdomen (a and c) and thorax (b and d). Images obtained while the patient is holding his/her breath may not be used for accurate radiotherapy treatment planning.](image-url)
Fig. 6. Body contours for a patient in supine and prone positions. The CT scan of the patient in supine position (Fig. 4b) is printed (life-size) and the contours taken from the scan in prone position (Fig. 4d) are superimposed showing large differences, particularly in the mediastinal region.

Random uncertainty is on the ninth figure. Because the random error is so small, physicists and radiotherapists are inclined to consider the calculations as exact, although large risks of error are associated with each step of the calculation.

Hardware errors are exceptional. For instance, there may be an error in memory addressing or a stray electrical signal interpreted by the computer as a code: the resulting errors in dose calculation are generally very large and can therefore be detected easily. However, there is a small chance of an undetected error.

Software errors are more frequent. They can occur, at any time, because of a typing mistake or as the result of incorrect programming but more often it is because of misinterpretation of the meaning of some terms. They can lead to large errors in dose calculation.

Samulski et al. [30] have assessed the accuracy of the methods used by radiotherapy centres to calculate the tumour dose along the beam axis for three reference cases: a rectangular field, a wedge field and an irregular mantle field. The errors found in the calculations exceeded the accepted criterion (5%) for 5, 15 and 23% of the participants for the three reference cases, respectively.

The use of sophisticated treatment plans implies that great care was taken checking the methods used for dose calculation.

To prevent such errors, a quality-assurance programme including initial and systematic checks, is mandatory. Initial checks should be used to compare the dose distribution of single beams with measured dose distributions and to test the beam model in extreme conditions such as very small or very large fields, large obliquities, use of wedge filters, or shielding blocks, etc. Repeated systematic checks should be carried out for a few typical treatment plans that are prepared to cover a wide spectrum of normal conditions and these should be carefully kept in order to check the reproducibility of the calculations.

One of the greatest advantages of the use of computers is to be able to provide dose distributions for treatment conditions for which manual calculations, such as three-dimensional calculation or irregular fields (Fig. 7), are not feasible. Without computers the doses to the parts of the target volume distant from the central plane or to the critical organs protected by shielding blocks could only be guessed. Thanks to computers the doses can be calculated with precision. However, there is a great danger in carelessly substituting an erroneous but impressive computer calculation for the correct guess of an experienced radiotherapist.

Nowadays the use of a computerised treatment planning system is often associated with the possibility to use CT scans as patient data. The CT-number distribution can be converted into electron-density distribution in order to correct the dose for the presence of lung, but to my knowledge, dose distributions were not and probably are still not corrected routinely for fat and bone and they are certainly only rarely corrected for soft tissue densities. The first question which arises regards the magnitude of the error encountered when tissues are assumed to be water-equivalent. Figure 8 shows the errors made on the absorbed dose as a function of the tissue thickness for three different beam energies: the higher the energy, the smaller the error.

Table III shows the errors made on the absorbed dose for three different beam energies and for typical errors in data concerning the patient. The errors made when no correction is applied for bone and fat, compensate approximately in that case, but they would not necessarily compensate in other
Fig. 7. 3-D dose distribution for a mantle field. A series of body contours is drawn in (a) together with a sagittal profile of the patient. The anterior and posterior mantle field contours are read out from the simulation radiographs (b) taking into account the magnification of the radiographs. They are also shown in a perspective view (c). The dose distribution can be computed in any transverse, frontal (d) or sagittal (e) plane for the last 10 years in the Institut Gustave Roussy.
situations as it is demonstrated for the head in Fig. 8.

Clinical experience has been gained throughout the world with dose calculations in water. Tumour doses stated in the literature are systematically in error by a few percent because of the fact that tissues are not equivalent with water. Performing inhomogeneity corrections in the physics department without giving the radiotherapist in charge of the patient clear warning could lead to systematic over- or underdosage of tissues, and then to failure to control the patient's disease. Systematic comparisons with in-water doses should be performed during a transitional period. However, if corrections are not performed when the necessary data and methods are available the desired precision improvement would not be attained.

The set-up of the patient

It is a complicated matter to ensure a stable and reproducible position of the patient during the whole treatment, from the treatment simulation to the first setting-up of the patient, and then from one treatment session to the next until the end of the treatment. To make matters more complicated, the localisation, simulation, planning and treatment are done with different instruments, at different times and by different personnel. The full benefit of the sophisticated methods used for patient data acquisition or for treatment planning, will be lost if this information cannot be transferred accurately to the therapy unit.

The position of the patient must be comfortable in order to be reproducible; there should be special supports under the knees, the neck or the shoulders, and also arm holders for breast cancer. Checks of the correct alignment of the whole patient with laser beams may help to ensure the reproducibility of the position. Careful analysis of the treatment portal films must be used, as in practice this is the only way to check the adequacy of the radiation fields to the target volume. Portal films are essential to improve the precision of the patient set-up at the time of the first session [23]. They do not, however, help to solve the difficulties arising from patient movement during treatment and the inability to set the patient in the same position relative to the beam, from session to session. The resulting errors are included in the concept of immobilisation error. In vivo dosimetry [2,29] is very useful for the estimation of the uncertainties related to both the set-up of the patient and the treatment unit parameters, including the beam modifiers such as wedge filters or shielding blocks.

Various techniques have been developed to guarantee accurate and reproducible positioning of the patient. No single technique can be valid for every tumour localisation, i.e. for head and neck tumours as well as for pelvis tumours. Furthermore, the position of a patient who is anxious during the first sessions, may be different from the position later, when the patient is relaxed.

In a good standard radiotherapy centre, where a quality-assurance programme is regularly applied, the setting of the patient form is generally the weakest point of the chain and largely contributes to the overall uncertainty.
TABLE III
Errors in the tumour absorbed dose induced by errors in patient data (tumour at 10 cm depth, field size 10 × 10 cm).

<table>
<thead>
<tr>
<th>Errors in patient data</th>
<th>Errors in absorbed dose</th>
<th>60Co (%)</th>
<th>6 MV (%)</th>
<th>25 MV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Error in tumour depth</td>
<td>± 0.5 cm</td>
<td>± 2.8</td>
<td>± 1.7</td>
<td>± 1.1</td>
</tr>
<tr>
<td></td>
<td>± 1</td>
<td>± 5.7</td>
<td>± 3.5</td>
<td>± 2.3</td>
</tr>
</tbody>
</table>

Maxillary
(1.5 cm, ρ = 1.65)
No correction          | + 5.5                    | + 3.4    | + 2.2    |
Error in bone thickness| ± 0.5 cm                | ± 1.8    | ± 1.1    | ± 0.7    |
Error in bone density  | ± 0.15                  | ± 1.3    | ± 0.8    | ± 0.5    |

Iliac bone
(3 cm, ρ = 1.3)
No correction          | + 5.1                    | + 3.2    | + 2.1    |
Error in bone thickness| ± 0.5 cm                | ± 0.9    | ± 0.5    | ± 0.35   |
Error in bone density  | ± 0.15                  | ± 2.6    | ± 1.6    | ± 1      |

Fat
(5 cm, ρ = 0.91)
No correction          | − 2.6                    | − 1.6    | − 1      |
Error in fat thickness | ± 0.5 cm                | ± 0.3    | ± 0.2    | ± 0.1    |

Intensive training of the technical staff, systematic rechecking of the adequacy of treatment portals during the course of treatment, the design of special devices for patient immobilisation for each type of tumour, all require a constant effort from radiotherapists and physicists in order to improve the overall precision in the dose delivered to the various parts of the tumour.

TABLE IV

<table>
<thead>
<tr>
<th>Origin of uncertainties</th>
<th>Main actions to reduce uncertainties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment unit parameters</td>
<td>Quality assurance programme</td>
</tr>
<tr>
<td>systematic uncertainties</td>
<td>Automatic check and control system</td>
</tr>
<tr>
<td>random uncertainties or mistakes</td>
<td>Periodical recalibration of the ionisation chamber at a Secondary Standard Laboratory</td>
</tr>
<tr>
<td>Absorbed dose measurement</td>
<td>Use of a published protocol</td>
</tr>
<tr>
<td>Patient data</td>
<td>Reject lead wires for body contour determination</td>
</tr>
<tr>
<td></td>
<td>Identical position of the patient for data determination and treatment</td>
</tr>
<tr>
<td></td>
<td>Use of CT scanner for internal structures whenever the patient can be set in treatment position</td>
</tr>
<tr>
<td>Treatment planning</td>
<td>Quality-assurance programme for the treatment planning computer used</td>
</tr>
<tr>
<td>Set-up of the patient</td>
<td>Intensive training of the staff</td>
</tr>
<tr>
<td></td>
<td>Verification by mean of treatment portals</td>
</tr>
<tr>
<td></td>
<td>In vivo dosimetry</td>
</tr>
</tbody>
</table>

Conclusion

The goal of radiotherapy is to eradicate a tumour without causing severe damage to healthy tissues. An overall precision of ±5% on the absorbed doses at any point in the patient is required to meet this goal. When looking into the long list of errors (Table IV) which may be encountered in the course of radiotherapy, the reduction of the overall uncertainty to the required level appears to be a challenge for the whole team of therapists, physicists, engineers and technicians. To differentiate between the responsibilities of the various members of the team is not the problem. It is much more important to convince everyone that a close cooperation is absolutely essential in order to achieve a significant decrease of the uncertainties.

I personally consider that delivering the present lecture illustrates that cooperation.

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