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Dose delivery uncertainty in photon beam radiotherapy

Arthur Curtin-Savard and Ervin B. Podgoršak

McGill University, Department of Medical Physics, Montreal General Hospital, Montréal, Québec, Canada

Even slight variations in total dose delivered to the patient in external beam photon radiotherapy can significantly alter the probability of tumour control and normal tissue complications. For this reason, the International Commision on Radiation Units and Measurements (ICRU) has recommended a goal of a ±5% precision in the dose delivered to the target volume. In this paper, we present the results of an uncertainty analysis which tracked the uncertainty in dose delivery through the entire radiotherapy process: calibration of the secondary standard, calibration of a field instrument, output determination of the treatment unit, measurement of beam parameters, calculation of an isodose distribution, calculation of the required machine setting, and the delivery of the radiation dose to the patient on the treatment machine. Our study finds cumulative beam intensity uncertainties of ±3.8 % (one standard deviation) and cumulative beam positional uncertainties of ±5.5 mm (one standard deviation). The effect of these uncertainties on the dose to the patient is illustrated on a typical case.

Key words: neoplasms-radiotherapy; radiotherapy dosage; photons

Introduction

Regardless of how sophisticated radiotherapy becomes, there will always be some uncertainty associated with the delivery of dose to the patient. The radiation dose delivered is influenced by the following elements: (1) calibration of the institution's secondary standard chamber at a national calibration laboratory; (2) calibration of a field instrument from the secondary standard chamber; (3) use of the field instrument in output determination for treatment units in the clinic; (4) measurement of beam parameters used in the calculation of the dose distribution and machine setting; (5) calculation of a dose distribution based on measured parameters and accounting for patient contour and tissue heterogeneities; (6) calculation of the machine setting for the daily fraction; and finally (7) patient set-up on treatment machine and possible patient or organ motion during treatment. It is important to determine the magnitude of the various contributions to the overall uncertainty; corrective efforts can then be applied efficiently to improve the accuracy of dose delivery and minimize the uncertainty.

Clinical studies[1, 2, 3] have shown that relatively small changes in the dose delivered to the patient in photon beam radiotherapy lead to appreciable changes in the probabilities both for tumour control and normal tissue complications. Although the dose-response curve varies with the type of disease treated, the ICRU[4] has recommended that institutions strive to deliver the dose to the target volume with an overall accuracy of ±5 % of the prescribed dose. This recommendation provided the motivation for a detailed uncertainty analysis undertaken at the Montreal General Hospital on photon beams produced by a Clinac-18 linear accelerator (10 MV beam) and a Theratron T-780 cobalt unit. In this paper we discuss the linear accelerator data; similar results and conclusions were obtained for the cobalt unit.

Correspondence to: Ervin B. Podgoršak, Ph. D., FCCPM, Director, Department of Medical Physics, Montreal General Hospital, 1650 avenne Cedar, Montreal, Québec, Canada, H3G 1A4. Fax: + 1 514 934 8229.

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Materials and methods

The uncertainty associated with each of the seven steps above was analyzed carefully and then combined to compute the overall uncertainty. We assume the uncertainties for the different steps to be uncorrelated which implies that the overall uncertainty is obtained by a quadrature summation of the individual uncertainties. This simple approach seems acceptable since there is considerable uncertainty on the uncertainty estimates themselves.

Except for step (1) which is in the hands of a national calibration laboratory and step (7) for which we referred to published studies, the uncertainty for each of the other steps listed above may be ascertained by examining the spread in results of repeated measurements of the quantity in question. The number of repetitions in our experiments was 30, with the uncertainty expressed as the standard deviation of the 30 measurements. A 0.6 cm^3 Farmer chamber (NE 2581) and a digital electrometer (Keithley 35617) were used in all experiments, except in the water tank scans where a 0.1 cm^3 water-proof ionization chamber was employed (Therados RK 83-05).

In order to obtain a realistic measure of the uncertainty for a given quantity, it is not sufficient to simply perform the set-up once and repeat the measurement thirty times, because the spread in measurement results is caused mainly by slight differences in set-up rather than by statistical variations in the measured parameter. Thus the set-up must be redone for each measurement. As an example, consider measuring the uncertainty on the wedge factor. Determination of the wedge factor involves taking the ratio of readings for a 10 × 10 cm^2 field at the depth of dose maximum (d_{max}) in phantom for the wedged field and the open field. For each measurement of the wedge factor, one must reset the field size, gantry angle, collimator angle, realign the chamber, and re-insert the wedge in the tray if one is to acquire a realistic uncertainty, representative of different measuring conditions.

Results

The secondary standard

The uncertainty on the cobalt-60 calibration factor for the secondary standard chamber provided by our national calibration laboratory[5] is 0.5 %. This is defensible since the precision of primary standards of cobalt-60 radiation, established through comparisons of numerous primary standards around the world,[6, 7] is within 0.3 % and the act of calibration introduces additional, non-negligible uncertainties.

Calibration of the field instrument

The calibration of the field instrument from the secondary standard chamber is performed in air by subjecting the two chambers to identical exposures in a cobalt-60 beam, and solving for the calibration factor, N_X^{field}, of the field instrument:

$$N_X^{field} = \frac{N_X^{sec} M^{sec}}{M^{field} P_{ion}^{field}} \quad , \qquad (1)$$

where N_X^{sec} is the calibration factor of the secondary standard chamber, M^{sec} and M^{field} are the meter readings of the secondary standard and field chamber, respectively, and P_{ion}^{field} accounts for recombination loss in the field instrument.

The uncertainty on the calibration factor of the field instrument can be deduced from the uncertainties on each of the variables in Eq. (1) using the usual quadrature summation. Experiments have shown that with normal care the uncertainty on readings taken in the calibration set-up with our chamber is about 0.07 %, reflecting the uncertainty on M^{sec} and M^{field}. If this estimate seems unusually low compared to typical clinical measurements, it is because in the calibration set-up the chamber is clamped to a rigid rod extending from the accessory tray which permits a highly-reproducible positioning. The uncertainty on P_{ion} for our chamber is less than 0.02 % and, as stated above, the uncertainty on the calibration of the reference chamber is 0.5 %. Combining these uncertainties with the uncertainties on the meter readings for each chamber gives a total uncertainty for the cobalt-60 calibration factor of our field chamber of 0.5 %, essentially attributed to the calibration factor of the secondary standard chamber.

Further analysis of the field instrument might include experiments to examine chamber response for dependence on polarity, angle of rotation and angulation, stem exposed to the beam, charge recombination, charge leakage, cable irradiation, and total dose. Extensive experimentation conducted prior to our uncertainty analysis confirmed that none of these effects is significant under typical conditions of use.

Output determination

The AAPM TG-21 dosimetry protocol[8] used in North America introduces a number of dose transfer coefficients and chamber-dependent correction factors by which the meter reading M obtained at a given depth in phantom must be multiplied to obtain the dose to medium at the same point:

$$D_{med} = MN_{gas}\left(\bar{\bar{L}}/\rho\right)_{air}^{med} P_{wall} P_{repl} P_{ion} \quad , \qquad (2)$$

where $\left(\bar{\bar{L}}/\rho\right)_{air}^{med}$ is the ratio of the restricted stopping powers for the medium material and air, P_{wall} is a correction factor dependent on the thickness and geometry of the chamber wall, P_{repl} is a gradient correction necessary for measurements not performed at d_{max} in phantom, and P_{ion} accounts for recombination loss. All of these factors are evaluated at the beam energy for which one is measuring D_{med}. The chamber-gas calibration factor, N_{gas}, is given by:

$$N_{gas} = N_X^{field} \frac{kW_{air}A_{wall}A_{ion}}{\left(\bar{\bar{L}}/\rho\right)_{air}^{wall}\left(\bar{\mu}_{ab}/\rho\right)_{wall}^{air}} \quad , \qquad (3)$$

where N_X^{field} was described in Eq. (1), k is a conversion factor from roentgen to C/kg (2.58×10^{-4} C/(kg•R)), W_{air} is the mean energy required to create an ion pair in air (33.97 eV/ion pair), A_{wall} is a correction factor dependent on the thickness and geometry of the chamber wall, A_{ion} accounts for recombination loss, $\left(\bar{\bar{L}}/\rho\right)_{air}^{wall}$ is the ratio of the restricted stopping powers for the chamber wall material and air, and $\left(\bar{\mu}_{ab}/\rho\right)_{wall}^{air}$ is the ratio of mass-energy absorption coefficients for air and the chamber wall material. All quantities in N_{gas} are evaluated at cobalt-60 photon energy.

Estimates of the uncertainties on the dose transfer coefficients are given in the literature[9,10] as follows: stopping power ratios are known to 0.6 %, while the mass-energy absorption coefficients and W_{air} are known to 0.2 %. The uncertainty on P_{repl} is estimated[11] at 0.2 %. From the TG-21 protocol,[8] we estimate the uncertainty on A_{wall} and P_{wall} to be 0.2 %. Uncertainties on A_{ion} and P_{ion} are negligible. From these values we calculate the uncertainty on N_{gas} for a typical field chamber to be about 1.0 %. Repeated measurements with a new set-up performed each time, have shown that the uncertainty on the meter reading, M, is 0.26 % for the 10 MV beam. Thus, combining the uncertainties on all factors in Eq. (2) gives an uncertainty of 1.2 % on the measurement of D_{med} at a given depth in phantom for our 10 MV beam.

The output of a treatment unit is generally defined as the dose rate to medium at d_{max} in phantom, for a 10×10 cm^2 field in units of cGy/min for a cobalt machine or cGy/MU for a linear accelerator. For output determination our institution employs a water phantom with an ionization chamber placed at 5 cm depth. The dose at d_{max} is then found by dividing the measured dose at 5 cm depth by the percent depth dose for a depth of 5 cm. With repeated measurements, we have established the uncertainty on percent depth dose measurements in a water tank to be around 0.5 %. This, combined with the 1.2 % uncertainty of the dose measurement at 5 cm depth, results in an output uncertainty of 1.3 %. Furthermore, the agreed upon tolerance of the output calibration is ±12 % which means that, frequently, the calibration can be off by over 1 %. This added uncertainty results in a cumulative uncertainty of approximately 1.8 % on the output of the 10 MV beam. In certain circumstances the output uncertainty may be even higher: for instance, with the use of highly-elongated fields because of the collimator-exchange effect or with very low monitor unit settings because of the monitor end-effect.

Input for the treatment planning system

For each field size in the range of fields sizes clinically employed, a treatment planning system typically requires percent depth doses and dose profiles at a number of depths in phantom as input for its dose calculation algorithm. The results of repeated water-tank scans (with a new set-up performed for each scan) revealed that the uncertainty on percent depth doses on the beam central axis and dose profiles well within the radiation field limits is of the order of 0.5 %. The uncertainty for dose profiles is considerably higher (~10 %) in the penumbra region because of the steep dose gradient in this region. For the percent depth doses, the uncertainty is negligible near d_{max} (since normalization is performed at this point) and slowly increases to reach about 0.8 % at a depth of 30 cm in the water phantom.

Dose distribution calculation

Uncertainties introduced in computerized treatment planning are the result of uncertainties in the beam data entered into the computer, imperfections in the calculation algorithm, and inaccuracies in the pa-

tient data which consists of body, organ, and target contours, as well as tissue heterogeneities. These factors can be expected to generate incongruities between calculated dose distributions and measured ones, with the act of measurement occasioning additional uncertainies. According to the ICRU:[12] "A computer-produced dose distribution can be considered to be accurate enough if it differs from relative dose measurements by less than 2 % (or 0.2 cm in position of isodose lines in special circumstances involving very steep dose gradients) in points of relevance for the treatment". However, a very comprehensive U.S. study[13] comparing six systems (using four different computational algorithms) found about a 3 % agreement (or 0.3 cm in position of corresponding isodose lines in regions of high dose gradient) for a wide range of test conditions. A Scandinavian study[14] tested the accuracy of six other systems in typical clinical situations and their results concurred with those of the U.S. study.

Calculation of machine setting

To calculate the machine setting from the physician's prescription, relative dose factors and wedge factors are needed in addition to the basic output calibration data. Reproducibility tests, once again, allowed us to conclude that the uncertainty on the relative dose factor is 0.3 % and the uncertainty on the wedge factor is 0.4 %.

Patient treatment

Concerning patient set-up, an extensive study by Rabinowitz,[15] as well as several studies of lesser scope,[16, 17, 18] were undertaken to assess the magnitude of positional uncertainties. These studies have found that the variability in patient position from one treatment fraction to another is about 3 mm, practically irrespective of site. Since these variations are random, their cumulative effect over the full course of treatment will be to increase the effective penumbra of the beam. Internal organ motion during irradiation is an additional positional uncertainty. A study of brain motion[19] has measured translations of 0.5 mm, which are negligible, while an estimate for the abdomen[20] is 4 mm. For thoracic irradiations, breathing and swallowing increase positional uncertainties still further.

The transfer of the patient from the simulator to the treatment couch also produces an uncertainty which the studies have found to be about 4 mm. Contrary to the inter-fraction positional uncertainties, this uncertainty occurs only once and thus has a systematic effect over the whole treatment course.

Discussion

The uncertainties in dose delivery described above naturally fall into two categories: beam intensity uncertainties and positional uncertainties. *Beam intensity uncertainties* encompass uncertainties attributed to the calibration of the field chamber, the output determination of the treatment unit, shortcomings of the treatment planning system, the quantities required in the calculation of the machine setting (relative dose factor and wedge factor), and variation in position of the patient along the beam axis. *Positional uncertainties* include variations in position of the patient across the beam and deficiencies of the treatment planning system in regions of high dose gradient, i.e., the beam penumbra.

To provide an example of the effect of the uncertainties on the dose delivered to a patient we have selected a typical three-field pelvic case with a prescription of 45 Gy to isocentre. For this case, beam intensity uncertainties yield a total of 3.8 % (one standard deviation). Positional uncertainties yield a total 5.5 mm (one standard deviation).

These uncertainties can be illustrated according to an approach suggested by Goitein.[21] Three dose maps are produced for the patient. A first map gives the nominal dose distribution; this is the dose distribution which we intend to deliver. A second map gives the largest possible dose that each point can receive; it is calculated with the beam weighting increased by 3.8 % and the field sizes increased by 5.5 mm on each of the four sides of the treatment fields. A third map gives the smallest possible dose that each point can receive; it is calculated with the beam weighting decreased by 3.8 % and the field sizes decreased by 5.5 mm on each of the four sides of the fields.

The three maps for our typical case are shown in Figure 1 where normalization is performed to give the dose in Gray. Points well within the field limits are affected only by the uncertainty on the beam intensity; for example, the isocentre dose, in comparison to the nominal dose of 45 Gy, may vary from 43.2 Gy to 46.8 Gy, or by ±13.8 % of the nominal dose. Points near a field limit suffer the effects of both the beam intensity uncertainties and the positional uncertainties. For instance, the nomi-

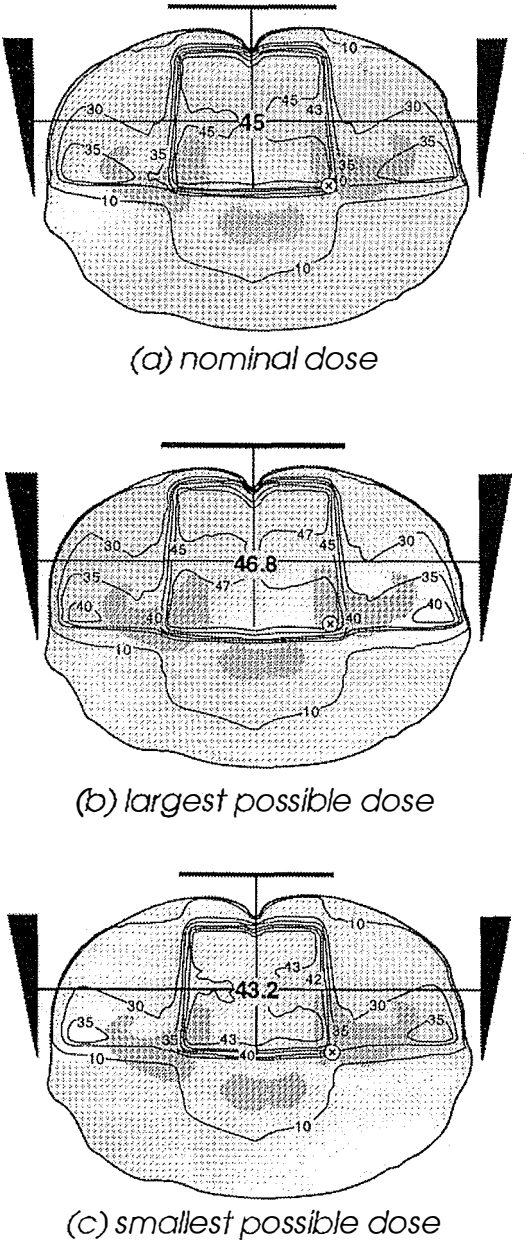

Figure 1. Effect of uncertainties in the radiotherapy process on the patient dose. For a typical example of pelvic irradiation with a three-field technique we show: (a) the nominal distribution, (b) the largest possible dose each point may receive, (c) the smallest possible dose each point may receive. Normalization is adjusted to give the dose in Gy. The isocentre dose may vary from 43.2 Gy to 46.8 Gy compared to the nominal 45 Gy, while the dose to a typical point in the penumbra region denoted by ⊗ may vary from 35 Gy to 47 Gy compared to the nominal 43 Gy.

nal dose delivered to the point denoted by ⊗ in Figure 1 is 43 Gy; because of the uncertainties the actual dose delivered to this point may vary from 35 Gy (−19 %) to 47 Gy (+9 %).

Conclusions

For the beam intensity uncertainties, our estimated total of 3.8 % (one standard deviation) is in conformity with the ICRU recommendation of ±5 % (if the ICRU recommendation is to be taken as one standard deviation). For the positional uncertainties, the 1 cm margin that physicians routinely add to all sides of the target volume would seem sufficient to account for the positional uncertainties of ±5.5 mm (one standard deviation) found in our study.

The uncertainties illustrated by the typical case shown above are representative of those associated with routine radiotherapy in the majority of modern centres; no special precautions are required to achieve this level of precision. Despite the partially subjective character of uncertainty estimates, other studies have come to very similar results.[20, 22, 23, 24] If the precision of dose delivery in radiotherapy is to be improved, treatment planning systems must become more sophisticated and better patient positioning devices must be developed. These two steps have been shown to be the major contributors to the overall uncertainty.

Since substantial variability also exists in medical diagnosis and dose prescription, further improvements in the accuracy and precision of radiotherapy will have to come both from the physical side and from the medical side. Yet the physical side plays a crucial role, for it is only when a high degree of accuracy and precision exists in the delivery of dose that clinical conclusions regarding the relative merit of different fractionation schemes, total doses, and normal tissue tolerance can be drawn.

References

1. Brahme A. Dosimetric requirements in radiation therapy. *Acta Rad Onc* 1984; **23:** 379–91.

2. Herring DF, Compton DMJ. The degree of precision required in the radiation dose delivered in cancer therapy. *Proceedings of the Third International Conference on Computers in Radiotherapy, Special Report No. 5* 1971.

3. Shukovsky LJ. Dose, time, volume relationships in squamous cell carcinoma of the supraglottic larynx. *Am J Roentgenol* 1970; **108:** 27–9.

4. 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 No. 24).* 1976.

5. National Research Council of Canada: Institute for National Measurement Standards. *Calibration of the NPL secondary standard dosemeter, model 2560, serial number 071, with the Nuclear Enterprises probe, model 2561, serial number 080: A document prepared for the Montreal General Hospital, report pirs-0484.* January 30, 1995.

6. Niatel M-T, Loftus TP, Oetzmann W. Comparison of exposure standards for Co-60 gamma rays. *Metrologia* 1975; **11:** 17–25.

7. Comparison of uncertainty estimates. *Comité consultatif pour les étalons de mesure des radiations ionisants (Section 1). CCREMRI (1) R(1)-9 BIPM.* 1985.

8. AAPM Task Group 21. A protocol for the determination of absorbed dose from high energy photon and electron beams. *Med Phys* 1983; **10:** 741–71.

9. Boutillon M, Perroche-Roux AM. Re-evaluation of the W for electrons in dry air. *Phys Med Biol* 1987; **32:** 213–9.

10. Andreo P. Uncertainties in dosimetric data and beam calibration. *Int J Radiat Oncol Biol Phys* 1990; **19:** 1233–47.

11. Attix F. A proposal for the calibration of plane-parallel ion chambers by accredited dosimetry calibration laboratories. *Med Phys* 1990; **17:** 931–3.

12. International Commission on Radiation Units and Measurements. *Use of computers in external beam radiotherapy: procedures with high-energy photons and electrons (ICRU Report No. 42).* 1987.

13. Masterson ME, Barest G, Chui C-S, Doppke KP, Epperson RD, Harms WB, Krippner KE, Mohan R, Slessinger ED, Sontag MR, Urie MM, Wallace RE, Wong JW. Inter-insitutional experience in verification of external beam photon dose calculations. *Int J Radiat Oncol Biol Phys* 1991; **21:** 37–58.

14. Kosunen A, Järvinen H, Vatnitskij S, Ermakov I, Chervjakov A, Kulmala J, Pitkänen M, Väyrynen T, Väänänen A. Intercomparison of radiotherapy treatment planning systems for external photon and electron beam dose calculations. *Radiother Oncol* 1993; **29:** 327–35.

15. Rabinowitz I, Broomberg J, Goitein M, McCarthy K, Leong J. Accuracy of radiation field alignment in clinical practice. *Int J Radiat Oncol Biol Phys* 1985; **11:**,1857–67.

16. Hunt MA, Kutcher GJ, Burman C, Fass D, Harrison L, Leibel S, Fuks Z. The effect of set-up uncertainties on the treatment of nasopharynx cancer. *Int J Radiat Oncol Biol Phys* 1993; **27:** 437–47.

17. Huizenga H, Levendag PC, De Porre PMZR, Visser AG. Accuracy of radiation field alignment in head and neck cancer: a prospective study. *Radiother Oncol* 1988; **11:** 181–7.

18. Hukku S, Das KJM, Nangia S, Kumar A, Ayyagari S. The use of portal images to study the accuracy of radiation field alignment and patient positioning in head and neck cancer. *Proceedings of the XIth International Conference on the Use of Computers in Radiation Therapy.* 1994; 268–9.

19. Enzmann DR, Pelc NJ. Brain motion: measurement with phase-contrast MR imaging. *Radiology* 1992; **185:** 653–60.

20. Svensson GK. Quality assurance in radiation therapy: physics efforts. *Int J Radiat Oncol Biol Phys* 1984; **10:** Suppl 1, 23–9.

21. Goitein M. Limitations of two-dimensional treatment planning programs. *Med Phys* 1982; **9:** 580–6.

22. Leunens G, Verstraete J, Dutreix A, van der Schueren E. Assessment of the inhomogeneity at target level by in vivo dosimetry: can the recommended 5 % accuracy in the dose delivered to the target volume be fulfilled in daily practice? *Radiother Oncol* 1992; **25:** 242–50.

23. Leunens G, Van Dam J, Dutreix A, van der Schueren E. Quality assurance in radiotherapy by in vivo dosimetry. 2. determination of the target absorbed dose. *Radiother Oncol* 1990; **19:** 73–87.

24. Svensson H. Quality assurance in radiation therapy: physical aspects. *Int J Radiat Oncol Biol Phys* 1984; **10:** Suppl 1, 59–65.