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EXTERNAL BEAM TREATMENT PLANNING

Can we deliver what we plan?

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Many sources of uncertainty exist in the delivery of the prescribed dose to the specified target volume in external beam radiotherapy. Their magnitudes are compared with recommendations for the overall accuracy of dose delivery (±5%). Five dose intercomparisons are reviewed, including a recent UK survey undertaken by the Institute of Physical Sciences in Medicine (IPSM). For phantom doses, standard deviations in the ratio of stated to delivered doses range from 1–3.5%, with larger uncertainties when irradiation of volumes within anthropomorphic phantoms is considered. In addition, uncertainties arise from geometrical discrepancies, and the role of portal films in their assessment is also considered. Imaging during radiotherapy will be increasingly important in the development of complex conformal treatments, where the shape of the target volume may be irregular.

Delivery of radiotherapy treatment has always been a three-dimensional procedure. For many years, however, the planning and visualisation of dose distributions has been carried out in only two dimensions, with multiple slices approximating the third dimension. Two major lines of development have made 3-D planning more feasible.

First, significant advances in imaging, principally through CT and, more recently, MRI (but also including grey-scale ultrasound and positron emission tomography) have been made. CT in particular is well established because of the detailed cross sectional information it provides and the ability to reformat contiguous slices into a pseudo-3D image array. MRI from this point of view is even better, since 3-D blocks of image data may be acquired with suitable pulse sequences showing isotropic spatial resolution. These techniques also have the advantage that their digitial format is amenable to transmission without degradation and to quantitation. Soft tissue contrast allows the visualisation of some tumours and aids the delineation of target volumes. Nishidai et al. (1) and Nagata et al. (2) have described the use of a CT scanner, in conjunction with a 3-D planning system, as a 'CT simulator' for scanning, dose calculation, simulation and optimization. The CT scanner is the source of multiple transverse slices, scanned projection radiographs and reconstructed 'beam's eye view' (BEV) images, together with optical delineation of field shapes on the patient's surface using a scanning laser.

Second, advances in linear accelerator design, such as asymmetric collimators, multileaf collimators, and computer control of these and other aspects of machine operation, have been made possible the planning and treatment of irregularly-shaped target volumes, using simultaneous variation of field size, position and angulation. Complementary treatment planning software allows the visualisation of three-dimensional target volumes and their coverage by BEV techniques. The integration of BEV images, together with digitised portal images and simulator radiographs, with a 3-D treatment planning system, has been described by McShan et al. (3). The rationale for this approach is that greater conformation to the target volume (itself prescribed more accurately from the improved imaging techniques) will enable tumour doses to be maximised and normal tissue doses to be minimised. A key question at this point is whether these calculated dose distributions

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can be delivered to the patient with acceptable dosimetric and geometric accuracy.

A problem with current treatment planning and delivery is the fact that the isodose display (which forms the basis for clinical judgements of acceptability) represents only an idealised 'snapshot' of the intended dose distribution in a particular plane. This review covers some of the most important sources of uncertainty in treatment delivery, in two broad categories, those of dose and geometry.

Sources of uncertainity in dose delivery

Several sources of uncertainity exist in the delivery of the prescribed dose to the specified target volume in external beam radiotherapy. Table 1 shows the combined (i.e. type A and type B) uncertainities (expressed as one standard deviation), associated with the 7 stages of dose delivery, adapted from Mijnheer et al. (4), although other estimates have been greater (e.g. 8.3% total uncertainty, (5) and 3.3% uncertainity arising from treatment machine tolerances only (6)).

The steepness of the dose–response and normal tissue damage curves can be used to deduce the acceptable uncertainty in dose delivery. Although the gradient of dose response curves varies markedly for different tumour types, it is possible to use the concept of the maximum probability of uncomplicated tumour control as a guide to the optimal dose and its associated uncertainty.

ICRU Report 24 (7) recommends an accuracy of $\pm 5\%$ in dose delivery to the target volume. Goitein (8) and Mijnheer et al. (4) have also suggested limits of $\pm 3.5\%$ (1 SD), the former attributing 1.5 standard deviations to the ICRU recommendation. It is clear that the estimated uncertainty of 4.2% is greater than the recommended limit and does not, moreover, include uncertainties in the definition of the target volume.

Table 1

Stage	Uncertainity (%)
Exposure calibration of ionisation chamber	1.4
Determination of absorbed dose at a reference point in a phatom	2.1
Determination of central axis dose distribution in a phantom	1.4
Patient topography	1.4
Calculation of absorbed dose at points within the patient	1.6
Dose monitoring	1.4
Patient irradiation	1.5
Combined uncertainty	4.2

* adapted from reference (4), combining Type A and Type B uncertainties in quadrature.

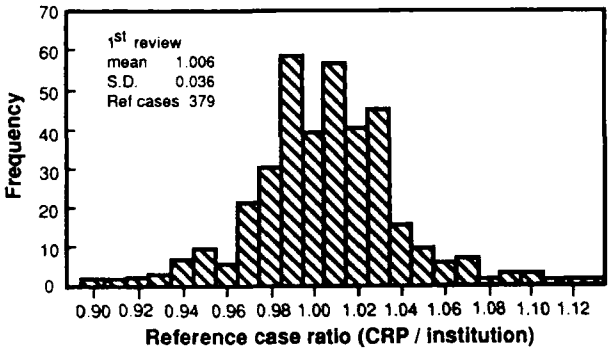

Fig. 1. Distribution of the ratio of determined dose to stated dose for x-ray tumour doses, from the North American survey (10). (Courtesy Dr Samulski and Int J Radiat Oncol Biol Phys).

One of the most powerful ways of estimating the combined effects of dose uncertainties is to conduct a dose intercomparison survey between radiotherapy centres. Several have been completed in recent years, the latest being a survey conducted by the Institute of Physical Sciences in Medicine (IPSM) in 64 U.K. radiotherapy centres (9).

North American survey (10). The frequency distribution of dose ratios in a review of 254 machines in the USA revealed a mean of 1.003 with a standard deviation of 2.7%. When more realistic tumour doses were calculated and compared with measurement, the standard deviation increased to 3.6% as shown in Fig. 1.

Scandinavian survey (11). An intercomparison amongst 23 Scandinavian centres with a total of 73 treatment machines was reported by Johansson et al. (11). The ratio of determined/stated absorbed doses for 4–45 MV x-rays showed a mean ratio of 1.017 with a standard deviation of 2.3%. These reduce to a mean of 1.004 with a standard deviation of 2.1%, if corrections for the use of different protocols are made. Similar results for electron beams are shown in Figs 2 and 3 for electron energies >10 MeV and <10 MeV respectively.

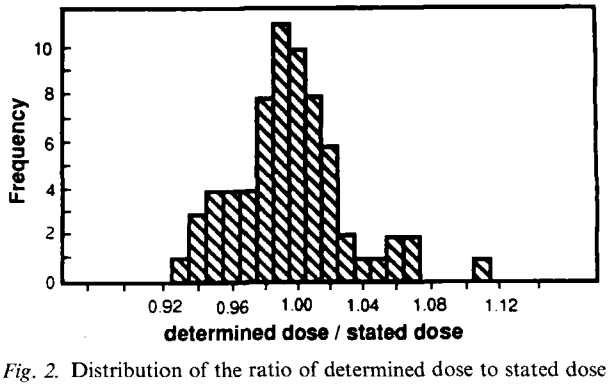

Fig. 2. Distribution of the ratio of determined dose to stated dose for electron beams >10 MeV, from the Scandinavian survey (11) $\bar{x} = 0.996 \pm 0.034$. (Courtesy Dr Johansson and Acta Radiol Oncol).

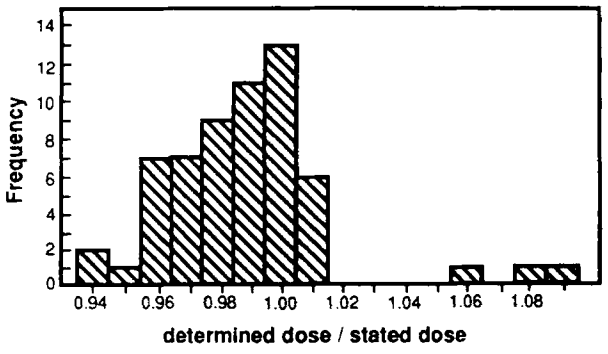

Fig. 3. Distribution of the ratio of determined dose to stated dose for electron beams < 10 MeV, from the Scandinavian survey (11). $\bar{x} = 0.989 \pm 0.027$. (Courtesy Dr Johansson and Acta Radiol Oncol).

EORTC survey (12). One of the criteria used in this survey was that the absorbed dose at specific points in a water phantom should be within $\pm 3\%$ of that stated by the radiotherapy centres. A variety of national and local protocols together with the use of both sealed and unsealed monitor chambers gave rise to variations of $\pm 3.2\%$ (1 SD) about a mean of 1.013 in the ratio of determined to stated dose for 4–25 MV x-rays.

Netherlands survey (13). In this survey, amongst other measurements, a simulated treatment of the prostate was undertaken using an anthropomorphic phantom and the calculated doses compared with measurements. The stated to measured dose ratio at the isocentre was 0.985 ± 0.015 and at 6 other points within the target volume it was 1.004 ± 0.52.

IPSM survey (9). This survey was carried out at all 64 radiotherapy centres in the U.K. The dose at a reference point at a depth of 5 cm was measured for several field sizes, together with dose at 5 other points within a planned, 3-field dose distribution. The distribution of the measured to calculated reference doses gave an average ratio of 1.003–0.015 (1 SD). For planned dose distributions, the range of measured to calculated dose ratios was 1.008 ± 0.027 and 1.008 ± 0.035 for water equivalent and lung inserts respectively. Discrepancies between calculated and measured doses of 5% or more were revealed in 9 of the centres.

Summary. Table 2 summarises the basic results of these intercomparisons. The magnitude of the standard deviations suggest that there is very little room for further uncertainty if tumour doses within $\pm 3.5\%$ (4, 8) are to be achieved. Most of this allowable uncertainty is already taken up with uncertainties in basic dosimetry for highly reproducible phantom irradiations. Where more realistic treatment simulations have been employed, standard deviations are, in general, greater, and may be up to $\pm 5\%$.

Geometrical discrepancies

In addition to dose uncertainties, geometrical discrepancies will arise from three main sources:
– those associated with treatment machine tolerances, (6) and uncertainties in size, shape and direction of the x-ray beams.

Table 2

Summary of surveys

	Dose ratio			
	(Reference conditions		Anthropomorphic phantom	
Survey	Mean	SD	Mean	SD
North American (10)	1.003	2.7%	1.006	3.6%
Scandinavian (11) (after correction)	1.004	2.1%	–	–
EORTC (12)	1.025 (sealed monitor chamber)	2.9%	–	–
	1.003 (unsealed monitor chamber)	3.5%		–
Netherlands (13)	0.996	1.1%	0.985	1.5%
			1.004*	5.2%*
IPSM (9)	1.003	1.5%	1.008*	2.7%*
			1.008**	3.5**

* Points within target volume.
** Points within target volume containing lung.

– uncertainties in the patient's position, including movement during a fraction, treatment set up errors and change of patient shape between fractions.
– uncertainties associated with internal tissue changes e.g. due to respiration or varying bladder volume. The latter class of discrepancies are particularly difficult to quantify, since soft tissue movement is difficult to visualise by portal imaging techniques, unless it is accompanied by related changes in easily imaged bone landmarks.

Svensson (14) has suggested spatial uncertainties of <5 mm (1 SD) arising from machine-related (<2.5 mm) and patient-related (<4 mm) displacements. Rabinowitz et al. (15) analysed simulator and portal films for 71 patients and found discrepancies in the position of anatomical landmarks on both films varying from 3.5 mm in the head and neck to 9.2 mm in the thorax. Sequential portal films were analysed and an average standard deviation of 3 mm found in field margins and block positions. Discrepancies between simulation and treatment are thus significantly greater than treatment-to-treatment variations at most sites. Table 3 illustrates the latter results and Figs 4 and 5 the discrepancies between the simulator and the last portal film for head and neck and pelvic treatments respectively.

Using a meticulous set-up procedure, Leong & Shimm (16) reduced the treatment-to-treatment variations to ± 1 mm, although not necessarily for all points within the field. This was achieved by taking portal radiographs before each treatment fraction and comparing them with those taken before the first fraction, adjusting the patient's position if required and repeating the portal imaging until co-incidence was judged to be satisfactory. The procedure took approximately one hour for each fraction. This is clearly impracticable for routine use in most radiotherapy departments, but is a valuable indication of the time and resources needed to make a significant improvement in geometrical accuracy. If positional accuracy of 1 mm really is necessary, it is not sufficient merely to ensure that this is achieved at the first fraction, since it is unlikely to be sustained throughout the complete schedule. On-line portal imaging could play a significant role in reducing the imaging time required, for those treatments where consistent millimeter accuracy is essential.

Entrance and exit measurements have been performed using semiconductor detectors (17). These illustrated the considerable influence of contour inaccuracies and tissue inhomogeneities. In 40% of check contours, the discrepancy between the contour used for planning and the actual patient diameter was >10 mm.

Large discrepancies of $>10\%$ between measured and expected transmission values were observed when the

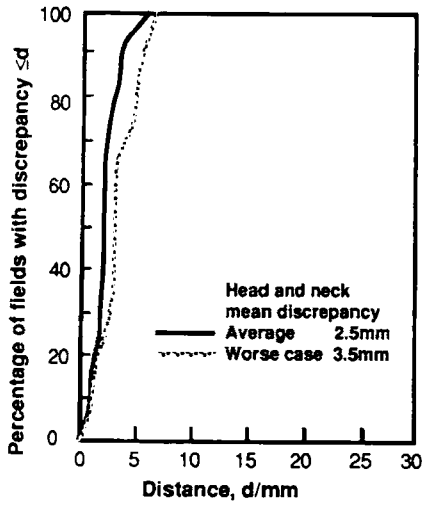

Fig. 4. Cumulative frequency distributions for discrepancies between the simulator film and last portal film for head and neck treatments (15). (Courtesy Dr Rabinowitz and Int J Radiat Oncol Biol Phys).

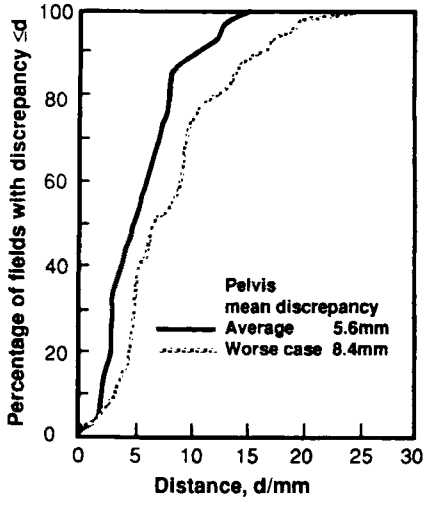

Fig. 5. Cumulative frequency distributions for discrepancies between the simulator film and last portal film for pelvic treatments (15). (Courtesy Dr Rabinowitz and Int J Radiat Oncol Biol Phys).

Table 3

Average treatment-to-treatment variation (standard deviation in mm) for combined retrospective and prospective routine clinical studies (from ref. 15). Average standard deviation of measurements (mm)

Site	Field margin	Customised blocks	Standard blocks
Brain	3.0		
Thorax	3.9	3.9	1.6
Abdomen	2.3	2.6	
Pelvis	2.0		3.2

Note: Measurements refer to the standard deviation of the distance from an anatomical landmark to the field margin or block. Data due to only one patient have been omitted. A more extensive analysis of the data can be found in reference (15).

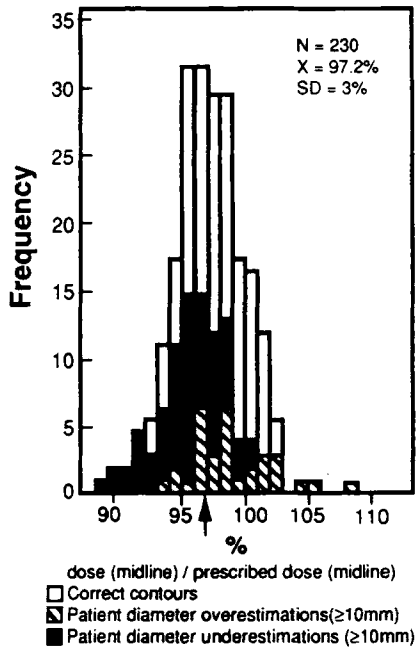

Fig. 6. Measured midline dose as a percentage of the prescribed midline dose (17). (Courtesy Dr Leuens and Radiother Oncol).

beam passed through bone structures. Fig. 6 shows the measured midline dose as a percentage of the prescribed midline dose and demonstrates a mean of 97.2 ± 3 (1 SD), due to contour errors, tissue inhomogeneities and inaccuracies in the treatment planning system algorithms.

An extension of this idea has been developed by Wong et al. (18) and Ying et al. (19) who have developed a portal imaging technique which can also be used to generate portal dose images, so that both dosimetric and geometric data can be acquired simultaneously. Several groups are pursuing on-line portal imaging with the intention of providing more comprehensive data, during treatment, of at least geometrical and possibly also dosimetric information (20–23). Some commercial designs are similar to that shown in Fig. 7 in which a television camera views a fluorescent screen via an angled mirror. A matrix ionisation chamber has also been designed (24). The discrepancies between simulator and portal films noted in (15) could be more accurately analysed if both sets of images were in digital format. The successful development of digital imaging in diagnostic radiology (e.g. photostimulable phosphors, digital image intensifier-TV systems) could also be exploited in the radiotherapy simulator (25, 26). Photostimulable phosphors have also been investigated as replacements for conventional x-ray portal films (27, 28) and digital processing of conventional film portal images has been investigated to improve visualisation of anatomical details (29, 30). Subtraction of the digital simulator image from the appropriately enhanced digital portal image could reveal geometrical discrepancies.

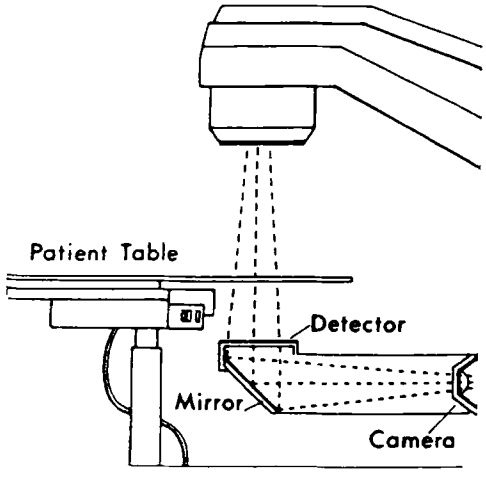

Fig. 7. A design for an on-line portal imaging system using fluorescent screen, angled mirror and TV camera.

Clincial variations

This brief review has concentrated on some of the physical uncertainities in treatment delivery. However, a broader perspective may be obtained by noting also the clinical variations in dose prescription. A recent survey by the Royal College of Radiologists (31) invited UK radiotherapists to consider six clinical problems and indicate the dose and fractionation schedule which they would normally prescribe. One of these cases is illustrated in Fig. 8. This shows the distribution of TDF values for the case of a 50-year-old

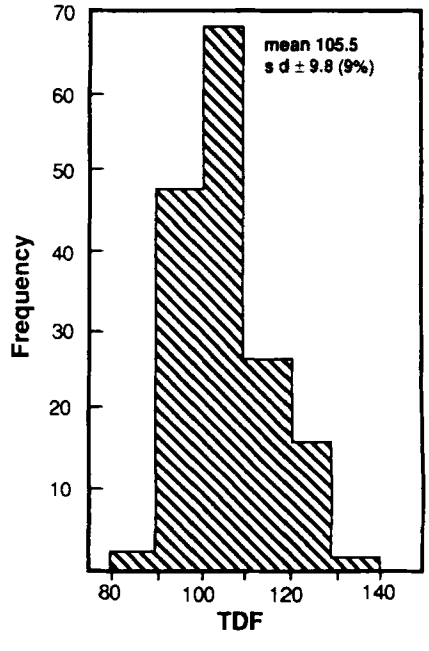

Fig. 8. Distribution of TDF values for the dose prescribed for a 50-year-old woman with a T1N0 squamous cell carcinoma of the right vocal cord. From RCR fractionation survey (31). (Courtesy Dr T Priestman and Clin Oncol).

woman with a T1N0 squamous cell carcinoma of the right vocal cord. Forty-seven different schedules were prescribed with total doses ranging from 33 Gy to 70 Gy. The TDF histogram shows a spread of ±9% (±1 SD). Other results showed standard deviations in TDF of 10% (for potentially curative treatments) to 26% (for palliative treatments).

Discussion

Current investigations of uncertainties in dose delivery have revealed values which are comparable to the recommendations of ICRU and others for the overall uncertainties. Further work on the refinement and standardisation of dosimetry protocols should reduce these further. On-line imaging should indicate when geometrical discrepancies arise and aid in their minimization, although significant and consistent improvements in accuracy are likely to be achieved only at the expense of greatly increased set-up time and a corresponding reduction in patient throughput.

Treatment planning systems are capable of producing 3-D dose distributions although their off-axis accuracy has yet to be fully evaluated. Moreover, treatment machines are capable of dynamic and conformal therapy for which accurate treatment planning algorithms have yet to be widely demonstrated. The potential benefits (higher tumour dose and/or lower normal tissue dose) can only be realised if the dose distributions associated with these complex plans can be accurately delivered. Current uncertainties in treatment delivery suggest that the goals of more complex conformal therapy might be compromised, unless more strenuous efforts are made to eliminate sources of error.

Specifically, the following are suggested as key areas in which progress should be made.

- dosimetry protocol standardisation,
- testing of treatment planning system algorithms, especially for off-axis, 3-D and inhomogeneity calculations,
- development of on-line portal imaging,
- development of transmission dosimetry in parallel with portal imaging,
- development of the digital simulator and/or the CT simulator and the capability for easy comparison of simulator and portal images.

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