Dosimetry in modern radiation therapy: limitations and needs

To cite this article: L John Schreiner 2006 J. Phys.: Conf. Ser. 56 1

View the article online for updates and enhancements.
Dosimetry in modern radiation therapy: limitations and needs

L. John Schreiner
Medical Physics Department, Cancer Centre of Southeastern Ontario, Departments of Physics and Oncology, Queen’s University, Kingston, ON, Canada

1. Introduction

1.1. Developments in Radiation Therapy
Despite the frequent view of the 1970’s that drug therapies would make radiation therapy redundant, its role continues to grow in the treatment of cancer. New patients treated in radiation clinics across Canada have more than doubled in the last two decades and approximately 50% of all cancer patients receive radiation therapy at some time during their illness [1,2]. About one quarter of these patients do not achieve local control, relapsing at the site of the primary tumour. Furthermore, the probability of metastatic disease may be linked to the local control [3,4]. It is thought that improvements in the practice of radiation therapy can improve local control and, hence, cure rates for cancer.

Radiation therapy is a localized treatment whose goal is to deliver a sufficient and uniform dose to the target to achieve tumour control while minimizing the dose to normal tissue to avoid complications. Over the years, external radiation therapy has improved by: i) the advance of high-energy linear accelerators with computer controlled multileaf collimators (MLCs) and on-line imaging, ii) the development of improved imaging to localize tumours for treatment planning, and iii) progress in treatment planning systems with more robust dose calculation algorithms and the incorporation of inverse planning modules. Brachytherapy has also advanced through improvements in delivery systems and in imaging for planning and for source localization.

Recent developments in radiation treatment have been motivated by the supposition that the therapy is improved by controlling radiation delivery so as to obtain a closer conformation of the delivered dose distribution to the target volume (see figure 1). Techniques developed to achieve this end are called three dimensional (3D) conformal radiation therapy techniques [5-8]. In external beam therapy (at a given photon energy), three main parameters may be manipulated to achieve a distribution that better conforms to the desired volume: the number and orientation of the radiation beams, the shape of each beam, and the intensity of the radiation within each beam. A special implementation of 3D conformal techniques, which manipulates all three of these parameters, is called Intensity Modulated Radiation Therapy (IMRT) [6-11]. While simple forms of IMRT using custom blocked fields with compensators or wedges have existed for decades, their use was limited to treatments with small numbers of fields and, some would argue, that this approach was not true IMRT since the field design from each orientation was usually not ‘optimized’ using inverse planning (see below) [6,8]. Recent development in IMRT has been to push forward the degree of automation, in particular through collimator design and computer control of linear accelerators (linacs). MLCs, linac output, gantry motion and couch motion must all be well characterized and controlled for the safe clinical implementation of IMRT [6,11-14]. Also computerized inverse treatment planning (in which beam
parameters are calculated using optimization algorithms and constraint criteria) is required to provide best design of the IMRT treatment parameters for a particular patient [6,8,11,12].

Multileaf collimators can be used in a number of different ways to achieve IMRT delivery [6,7,11,14,15]. In the ‘step & shoot’ technique the MLC is positioned and the beam is turned on for a period of time after each field shape is set. Dynamic IMRT can be achieved with a movable MLC with the beam ‘on’ during the motion in an approach similar to the dynamic wedge. Therapy with multiple arcs of uniform intensity MLC shaped beams provides a hybrid form of static and dynamic IMRT. Helical tomotherapy (literally, slice therapy) is an innovative IMRT [16-19] modality incorporating a linac in a CT scanner like gantry. It provides conformal delivery through the fluence modulation of a thin fan beam as it revolves about a patient that is translated though the gantry plane. The tomotherapy unit also incorporates a detector system enabling megavoltage CT (MVCT) imaging at time of treatment for patient registration and, potentially, dose delivery verification through reconstruction of exit dose data acquired during beam delivery. One could argue that the intensive development of IMRT capabilities on conventional commercial linacs was motivated in a large part by the intensity modulation potential indicated by tomotherapy. As an aside, our group in Kingston has shown that tomotherapy is feasible using a cobalt radiation source in the place of a linac [20].

![Image](image1.png)

**Figure 1.** A simple analogy (from woodcarving) for the evolution to conformal radiation therapy.

The target treated by radiation often has a complex shape. The high dose volume can be shaped closely to the convex and concave extensions of the target by increasing the number radiation beam directions and by IMRT (see text).

![Image](image2.png)

**Figure 2.** Radiation delivery must be more precise in conformal therapy. The 1970’s conventional rectangular field (gray border) with a good margin would irradiate the target (black) even if the field was shifted. Similar shifts in the conformal delivery result in missed tumour.
The dose distributions delivered during 3D conformal therapy and IMRT are specifically designed to fit tightly about the target volumes and so are characterized by sharp dose gradients, particularly in the transition region between the target and healthy normal tissue. Thus, the possibility of missing the target, because of patient setup errors, organ motion, or even small fluctuations in treatment delivery, increases (see figure 2), and great care is required to determine appropriate margins about the target volumes to be irradiated, to reproduce treatment setup for each of the multiple visits the patient makes in the course of treatment, and to verify that the dose administration is as intended. A major body of medical physics and radiation oncology research in the last decade has been to develop techniques for describing treatment volumes and dose prescriptions [21], to assess population and patient specific margins for treatment [22-26], and to develop appropriate treatment setup monitoring strategies [27-29].

While there are some who question the benefits of conformal and IMRT approaches [30-32], it is clear that these techniques are becoming standards of practice and that a significant proportion of patients may benefit from IMRT techniques' potential to increase tumour dose while maintaining, or even decreasing, the level of normal tissue complications [3,6,33]. Results from clinical trials seem to bear this out in the prostate [34,35]. The evaluation of IMRT at specific clinical sites has been based primarily on studies comparing various treatment planning parameters (such as dose-volume histograms, dose statistics, normal tissue complication probabilities, tumour control probabilities, etc.) with those calculated using conventional or alternate conformal techniques. This technical evaluation approach has been used for various sites including prostate [36-39], head and neck [40-43], brain [44] and lung [45].

Imaging immediately prior to radiation therapy is being developed as an important aspect of ensuring patient, and session, specific conformal delivery [46-48]. Approaches include megavoltage image on treatment units with electronic portal imaging devices, kilovoltage imaging and ultrasound. On-line computed tomography imaging has also become prominent in this work [49-52], including MVCT imaging in helical tomotherapy [53,54]. Such image guided radiation therapy (IGRT) has

**Figure 3.** The process of adaptive radiation therapy (see text) in image guided tomotherapy. The two aspects indicated in the frames with heavy borders are inherent with the rotational geometry of tomotherapy. Image guidance at treatment is achieved through MVCT of the patient. If the patient setup agrees with the treatment planning then treatment can proceed directly. If not then the patient can be moved or the treatment plan can be modified. One implication of this approach is that target margins can be reduced as patient specific information is available.
been shown to be effective in ensuring correct patient setup and positioning during delivery. More relevant to us, IGRT seems to help reduce the margins required around targets during treatment, since the margins can now be patient specific rather than population based [54-56].

These developments have also advanced into a process termed adaptive radiation therapy in which patient setup or radiation delivery is modified throughout a patient’s treatment course using systematic feedback of various imaging and, perhaps, dose measurements made immediately prior, or during, treatment [57-59]. Figure 3 shows one particular schema for adaptive radiation therapy in the tomotherapy setting. The process of adaptive therapy is intended to ensure that the potential dosimetric advantages of conformal IMRT (conformal dose targeting with possible dose escalation) are well achieved for each particular patient. The tomotherapy implementation of adaptive radiation therapy is not restricted to correction of patient setup and geometry alone; the actual radiation delivery can also be monitored and, perhaps, corrected in subsequent delivery [60]. However, the processes of optimization, imaging and dose verification are not independent [53], and further validation, perhaps with independent dose measurements, is likely necessary to establish the robustness of dose correction adaptive treatment process.

Finally, the development of radiation therapy is advancing further with four dimensional treatment approaches intended to account for the motion of the target inherent in the treatment of particular cancers. Briefly, these are adaptive techniques in which the radiation is gated to ensure dose delivery when the target is positioned at the radiation aperture [61,62] or the aperture is steered to follow the motion of the target [63,64]. The perceived advantage of these techniques is again the reduction of target margins by the gating or tracking [65]; however, the magnitude of the dosimetric and geometric uncertainties associated with the motion must be assessed carefully for the specific cancer site to establish the advantage over conventional treatment [62].

1.1.1. Implications for radiation dosimetry

From the discussion above it should be already apparent that the dose distributions delivered by conformal IMRT are complex; with large dose drop-off in small spatial displacement at the edge of the targets and often with non-uniform doses in the target volume [7,12] (depending on the proximity of organs at risk). Furthermore, the doses are delivered dynamically (as illustrated in figure 4) so that

**Figure 4.** Four frames illustrating the dynamic nature of IMRT, here via Co-60 tomotherapy, dose delivery required to achieve the distribution at right. In each pair the right hand image shows the instantaneous fan beam modulation pattern required at specific orientations (given in degrees; white indicating greater dose / fluence). The left hand image shows the total dose as the delivery progresses. The desired dose distribution is achieved after a complete rotation about the patient.

The gray scale changes with each image to maintain dynamic range.
specific points in the irradiated volumes may receive their final dose only over a total treatment time. From these two features alone, it is clear that the dose verification for IMRT will be inherently arduous, as the data will have to be sampled with good spatial resolution over some measurement volume using integrating dosimeters.

One other feature of IMRT treatment introduces further implications for the dosimetry and delivery verification required for clinical practice: the treatment planning and the generation of the control parameters for the radiation delivery [6-8,11,12,14,15,66,67]. IMRT treatment planning systems incorporate much more sophisticated photon and charged particle transport algorithms than the empirically based systems typically used only a decade ago. This is in part to enable robust modelling in the heterogeneous media making up the patient anatomy. Also, inverse planning is required for IMRT to establish the dose delivery parameters to control the linac [8,12,68]. This presents two challenges: the results of the inverse planning depend critically on the definition of: i) the target structures and organs at risk [13], ii) the dose constraints set for these structures and iii) other parameters used to direct the progress of the optimization [12,68]. Also to ensure timely calculations, treatment planning systems may use simplified calculations during the majority of optimization iterations determining the fluence patterns required to achieve the dose distributions satisfying the constraint criteria, with a more robust dose calculation algorithm used only in a final calculation or set of iterations [12]. These points may lead to a final plan that does not provide the best possible IMRT delivery for a particular patient. While this may not be strictly a concern for dose validation, there are definitely training implications for dosimetrists, physicists, and radiation oncologists. Also, in some commercial planning systems a separate leaf sequencing (or translation) algorithm is run after the fluence optimization to determine the MLC trajectories required during treatment to deliver the ‘optimized’ fluence pattern. This does become a dose validation issue, as the integrity of the dose distribution under particular leaf sequences may be sensitive to practical characteristics such as the type of MLC delivery used, the monitor units (MU) required to deliver each subfield (often limited to low MUs), the size of individual subfields (perhaps introducing uncertainties from small field dosimetry at commissioning), the integrity of the commissioning dose data at leaf edges [69], etc. Thus, the fluence under the MLC sequence (and, subsequently, the resulting dose distributions and the summary dose data presented by various statistical dose evaluation tools) may be perturbed from those presented at the end of the treatment planning system optimization [11]. Furthermore, there may no longer be an intuitive direct relationship between the prescribed dose and the number of MUs required to complete the treatment [7,14]. Thus MU checking is critical to ensure that the final treatment plan/prescription (MLC trajectory with MU calculation) delivers the intended dose and dose distribution. Because of this, Galvin [12] and others recommend: i) an independent calculation of the monitor units using a secondary calculation system ideally based on independent beam characterization, and ii) validation absolute dosimetry at some reference point in the irradiated volume with relative dosimetry to verify the distribution throughout the volume [7,12,14,66,68,70,71]. Historically this is achieved by irradiating a regular phantom containing an ion chamber and film using the patient specific planned fluence patterns [70,72]. This can be very labour intensive and alternate point (e.g., MOSFETs, scintillation detectors, TLDs [73-75]) and 2D dosimetry approaches (e.g., ion chamber or diode arrays [76-79]), scintillator screens [80], portal image devices [81-84] have been proposed (see review article by Kevin Jordan in these proceedings).

2. The Challenge of IMRT Dosimetry

The discussion above establishes the importance of appropriate dosimetry for intensity modulated radiation therapy and helps set the various components of dosimetric measurement and quality assurance required for clinical implementation of IMRT. The dosimetric validation is required to ensure i) that the dose distributions calculated and optimized by the treatment planning system, along with the monitor unit determinations for the various fields, are correct, and ii) that the dose delivery is achieved (that is, ensuring that the transfer of control data from the treatment planning system to the linear accelerator and the subsequent complex machine operation during irradiation are correct).
The dosimetry validation is typically achieved through a series of different dose measurements performed at specific phases of the IMRT implementation [6,7,11,12,14,85,86] (see table 1). In the first phase, initial radiation beam characterization and commissioning data are collected on the linac and input into the treatment planning system. Once the system is commissioned, treatment planning and delivery should be performed on simple flat or cylindrical (and, perhaps, anthropomorphic) phantoms in order to validate that the IMRT process operates correctly. This step should be implemented each time a new IMRT treatment protocol is established in the clinic, such as, when IMRT delivery is extended to a new cancer site. During this process, well defined test cases should be run to establish results which can be used as benchmarks for the comparison of future QA test results. Once the IMRT planning and delivery have been fully commissioned and tested, one can commence the second phase of the regular dosimetry required to ensure the integrity of treatment planning and of dose delivery [87]. Typically, this involves repeating the planning of standard cases and performing dose measurements of the related delivery performed on a phantom. The results from this regular QA should be compared to those benchmarked in the testing performed during phase 1. The third phase of dosimetry validation is the verification of patient specific treatment. Currently, this typically includes two main components. In the first, the monitor units calculated by the treatment planning system are verified, either by an independent validated computer application, or by measurement in phantom.

Table 1. A summary of some of the dose measurements and validation experiments required for implementing IMRT.

| Phase and Intent | Dosimetry / Test Required | Typical Tools and Approaches | Role for Gel Dosimetry |
|------------------|---------------------------|------------------------------|------------------------|
| 1. Commissioning of treatment planning system and benchmarking of performance (both treatment planning and dose delivery) | Acquisition of beam data to dosimetrically characterize beam, machine data to mechanically characterize linac. Measurement of test cases planned in phantom under well defined conditions to ensure correct performance and establish benchmark data for each particular treatment protocol. | Ion chamber (including micro chambers), water tank, film, detector arrays Regular and anthropomorphic phantoms; film; 2D dose QA systems (ion chamber and diode), portal imaging systems | no yes |
| 2. Periodic QA | Routine testing of the delivery system; QA to ensure continued planning and delivery as at commissioning | Regular and anthropomorphic phantoms; film; 2D dose QA systems (ion chamber and diode), portal imaging systems | yes |
| 3. Routine patient specific treatment QA | QA of Monitor Unit (MU) calculations Testing of delivered dose distributions At treatment measurement of delivered dose and dose distribution. | Independent validated calculation system or direct measurements in phantom (see cell below) with ion chambers or other point dosimeters Replace patient by standard phantom, expose phantom to same MLC sequence, trajectories and MUs as for patient. 2D dosimeters In-vivo dosimetry or online exit beam dosimetry (using EPID or tomotherapy imaging detector) | possibly yes no |

For the dose measurement, the patient’s treatment plan is run on the image data for a simple test phantom designed with specific locations into which point detectors can be placed for verification. The validation should also extend to verification of the dose distribution delivery. Again this is done in phantom but with (typically) 2D dosimetry systems (film or detector arrays) [88]. In some centres, the distributions are assessed by confirming the fluence pattern of the individual fields irradiating the phantom, although dose can be measured using a composite irradiation with all planned fields. The advantage to the former approach is that errors in delivery can be identified directly with a specific field condition [76]; however, the approach is more laborious as each field must be set up and
irradiated. Finally, dose validation can be done at the time of patient irradiation: currently, using in-vivo dosimetry [75] and, in the future once radiation devices develop more fully for adaptive radiation therapy, by dose reconstruction from exit beam data measured during the treatment delivery [53,81,89].

One final component of the dosimetry validation should be discussed: the evaluation of the dose QA results, particularly in the verification of dose distributions. Many of the tests in table 1 will lead to large 2D and, perhaps, 3D data sets that are to be compared with planned dose data. Thus, the evaluation may be complex and require specific software tools for data registration and comparison [11,90,91]. The approach of one decade ago of overlaying dose contours may be sufficient if the contours agree, but is not easily interpreted if agreement fails. Dose difference maps can be generated that display regions where measurements disagree with calculation [92]. However, such maps are overly sensitive to differences in high dose gradients, since small spatial errors in either data set can lead to large dose differences between the measured and planned distributions [93]. To moderate this flaw, distance to agreement (DTA) maps were proposed; these display the distance between a measured dose point and the nearest dose point in agreement in the calculated dose distribution [90,93]. While DTA maps give a better comparison of dose in high dose gradient regions than the dose difference, they tend to be overly sensitive in regions of relatively uniform dose (low dose gradients). That is, large DTA values may be calculated even for small dose differences [90,94]. Since these two measures are overly sensitive in different regions of the dose distributions, Harms suggested that both measures be used together in dose distribution validation [90] by plotting regions of failure for each test on a composite plan. Low formalized this line of approach in the development of the gamma dose distribution method [91,94-96]. Essentially the gamma function quantifies the dose and distance agreement measures by assigning a value of 1 or less to regions where dose or distance to agreement are within some set criteria (often set as agreement within 3% in dose and 3 mm in distance), and a value of greater than 1 in regions where the evaluations disagree [91,94,96]. (Note that the 3%/3mm acceptance criteria are consistent with the dosimetry criteria cited by Van Dyk [93] and the AAPM task group 53 [97], and others [67].) The gamma function is usually plotted as a colour wash. There are some limitations to the original Low approach [95,96], however, the gamma function has shown itself to be a good evaluation tool to compare measured-to-planned dose distributions [83,88,98-101] or dose distributions measured using different dosimetry techniques. One approach for reporting the agreement of planned and measured dose delivery has been to use the percent of pixels failing the gamma function test as a metric [102]. Other methods have also been suggested for dose distribution comparisons [11] (for example dose difference histograms, comparisons of measured and planned dose volume histograms, requiring the specification of structures on both distributions being compared). However, in some of these approaches one loses the spatial information specifying, for example, the regions of disagreement.

3. Conclusion
As noted a number of times, the complex nature of the treatment planning and beam delivery required for IMRT, and the conformal nature of the resulting dose distributions, make dosimetry validation time consuming (although the new 2D array devices will likely increase efficiency of some tests). The challenge of dose verification will likely become more severe in the future, with the development of 4D radiation therapy to accommodate target motion, since the dosimetry validation will have to be done with phantoms undergoing motions mimicking those encountered clinically. Also, one can foresee a time when the intent of radiation treatment will be to irradiate parts of the target to variable non-uniform doses, perhaps because of information gained from biological/functional/molecular imaging [15,103]. Thus, the limitations of conventional dosimeters will likely increase with the further adoption of 4D IMRT and IGRT. This prospect, together with the attractive characteristics of gel dosimeters (such as high spatial resolution, tissue equivalence [104], direct 3D dose measurement, absolute and relative dose capabilities, etc.) spurred the development of gel dosimetry [67,86,105-107]. The possible role of gel dosimetry in IMRT validation is summarized also in table 1.
The intent of this introductory chapter has been to extend the motivation for gel dosimetry beyond the discussion of solely radiation measurement. The issues of dosimetry had already been well presented in similar reviews in the proceedings of the three previous DosGel conferences [67,86,107]. I have tried to provide the context for this 2006 DosGel Conference in Sherbrooke by presenting a broad review of the developments in modern conformal radiation therapy using intensity modulation, image guidance and adaptive processes. With this motivation, I invite you to enjoy the remainder of the review and proffered papers from this meeting. These present an excellent record of the fundamental science of gel dosimetry and exciting reports of the current state of field.

4. References

[1] Usmani N, Foroudi F, Du J, Zakos C, Campbell H, Bryson P et al. 2005 An evidence-based estimate of the appropriate rate of utilization of radiotherapy for cancer of the cervix. *Int J Radiat Oncol Biol Phys* 63 812-27

[2] Foroudi F, Tyldesley S, Barbera L, Huang J and Mackillop W J 2003 Evidence-based estimate of appropriate radiotherapy utilization rate for prostate cancer. *Int J Radiat Oncol Biol Phys* 55 51-63

[3] Leibel S A, Ling C C, Kutcher G J, Mohan R, Cordon-Cordo C and Fuks Z 1991 The biological basis for conformal three-dimensional radiation therapy. *Int J Radiat Oncol Biol Phys* 21 805-11

[4] Leibel S A, Scott C B, Mohiuddin M, Arcial V A, Coia L R, Davis L W et al. 1991 The effect of local-regional control on distant metastatic dissemination in carcinoma of the head and neck: results of an analysis from the RTOG head and neck database. *Int J Radiat Oncol Biol Phys* 21 549-56

[5] Webb S 1993 The Physics of Three-Dimensional Radiation Therapy. Mould R F, Orton C G, Spaan J A E and Webster J G, editors. (Bristol, UK, IOP Publishing Ltd)

[6] IMRT Working Group 2001 Intensity Modulated Radiotherapy: Current Status and Issues of Interest. *Int J Radiat Oncol Biol Phys* 51 880-914

[7] Ezzell G A, Galvin J M, Low D, Palta J R, Rosen I, Sharpe M B et al. 2003 Guidance document on delivery, treatment planning, and clinical implementation of IMRT: report of the IMRT Subcommittee of the AAPM Radiation Therapy Committee. *Med Phys* 30 2089-115

[8] Webb S 2003 The physical basis of IMRT and inverse planning. *Br J Radiol* 76 678-89

[9] Bortfeld T, Boyer A L, Schlegel W, Kahler D L and Waldron T J 1994 Realization and verification of three-dimensional conformal radiotherapy with modulated fields. *Int J Radiat Oncol Biol Phys* 30 899-908

[10] Boyer A L and Yu C X 1999 Intensity-modulated radiation therapy with dynamic multileaf collimators. *Semin Radiat Oncol* 9 48-59

[11] Ahnesjo A, Hardemark B, Isacsson U and Montelius A 2006 The IMRT information process-mastering the degrees of freedom in external beam therapy. *Phys Med Biol* 51 R381-R402

[12] Galvin J M, Ezzell G, Eisbrauch A, Yu C, Butler B, Xiao Y et al. 2004 Implementing IMRT in clinical practice: a joint document of the American Society for Therapeutic Radiology and Oncology and the American Association of Physicists in Medicine. *Int J Radiat Oncol Biol Phys* 58 1616-34

[13] McNair H A, Adams E J, Clark C H, Miles E A and Nutting C M 2003 Implementation of IMRT in the radiotherapy department. *Br J Radiol* 76 850-6

[14] Williams P C 2003 IMRT: delivery techniques and quality assurance. *Br J Radiol* 76 766-76

[15] Bortfeld T 2006 IMRT: a review and preview. *Phys Med Biol* 51 R363-R379

[16] Mackie T R, Holmes T, Swerdloff S, Reckwerdt P, Deasy J O, Yang J et al. 1993 Tomotherapy: a new concept for the delivery of dynamic conformal radiotherapy. *Med Phys* 20 1709-19

[17] Mackie T R, Balog J, Ruchala K, Shepard D, Aldridge S, Fitchard E et al. 1999 Tomotherapy. *Semin Radiat Oncol* 9 108-17
[18] Olivera GH, Shepard DM, Ruchala KJ, Aldridge JS, Kapatoes J, Fitchard EE et al. Tomotherapy. In: Van Dyk J, editor. The Modern Technology of Radiation Oncology. Madison, Wisconsin: Medical Physics Publishing, 1999: 521-587.

[19] Mackie T R 2006 History of tomotherapy. Phys Med Biol 51 R427-R453

[20] Schreiner LJ, Kerr AT, Salomons GJ, Dyck C, Hajdok G. 2003 The Potential For Image Guided Radiation Therapy With Cobalt-60 Tomotherapy. Proc. 6th Annual International Conference on Medical Image Computing and Computer Assisted Intervention (Springer, Heidelberg, Germany) 449-456.

[21] International Commission on Radiation Units and Measurements 1999 Prescribing, Recording and Reporting Photon Beam Therapy (Supplement to ICRU Report 50). 62 (Bethesda, MD, International Commission on Radiation Units and Measurements)

[22] Dawson LA, Mah K, Franssen E and Morton G 1998 Target position variability throughout prostate radiotherapy. Int J Radiat Oncol Biol Phys 42 1155-61

[23] Zelefsky M J, Crean D, Mageras G S, Lyass O, Happersett L, Cliffton Ling C et al. 1999 Quantification and predictors of prostate position variability in 50 patients evaluated with multiple CT scans during conformal radiotherapy. Radiother Oncol 50 225-34

[24] Yan D, Lockman D, Brabbins D, Tyburski L and Martinez A 2000 An off-line strategy for constructing a patient-specific planning target volume in adaptive treatment process for prostate cancer. Int J Radiat Oncol Biol Phys 48 289-302

[25] Amer A M, Mackay R I, Roberts S A, Hendry J H and Williams P C 2001 The required number of treatment imaging days for an effective off-line correction of systematic errors in conformal radiotherapy of prostate cancer — a radiobiological analysis. Radiother Oncol 61 143-50

[26] Bortfeld T, van Herk M and Jiang S B 2002 When should systematic patient positioning errors in radiotherapy be corrected? Phys Med Biol 47 N297-N302

[27] Pisani L, Lockman D, Jaffray D, Yan D, Martinez A and Wong J 2000 Setup error in radiotherapy: on-line correction using electronic kilovoltage and megavoltage radiographs. Int J Radiat Oncol Biol Phys 47 825-39

[28] Alasti H, Petric M P, Catton C N and Warde P R 2001 Portal imaging for evaluation of daily on-line setup errors and off-line organ motion during conformal irradiation of carcinoma of the prostate. Int J Radiat Oncol Biol Phys 49 869-84

[29] Morr J, DiPetrillo T, Tsai J S, Engler M and Wazer D E 2002 Implementation and utility of a daily ultrasound-based localization system with intensity-modulated radiotherapy for prostate cancer. Int J Radiat Oncol Biol Phys 53 1124-9

[30] Schulz R J 1999 Comment on "Intensity-modulated conformal radiation therapy and 3-dimensional treatment planning will significantly reduce the need for therapeutic approaches with particles such as protons" Med Phys 26 2515

[31] Schulz R J and Kagan A R 2003 More precisely defined dose distributions are unlikely to affect cancer mortality. Med Phys 30 276

[32] Donaldson S S and Boyer A L 2000 New methods for precision radiation therapy exceed biological and clinical knowledge and institutional resources needed for implementation. Med Phys 27 2477-9

[33] Keall P J and Williamson J F 2003 Clinical evidence that more precisely defined dose distributions will improve cancer survival and decrease morbidity. Med Phys 30 1281-2

[34] Leibl S A, Zelefsky M J, Kutcher G J, Burman C M, Kelso S and Fuks Z 1994 Threedimensional conformal radiation therapy in localized carcinoma of the prostate: interim report of a phase I dose-escalation study. J Urol 152 1792-8

[35] Horwitz E M, Hanlon A L and Hanks G E 1998 Update on the treatment of prostate cancer with external beam irradiation. Prostate 37 195-206

[36] Zelefsky M J, Fuks Z, Hunt M, Yamada Y, Marion C, Ling C C et al. 2002 High-dose intensity modulated radiation therapy for prostate cancer: early toxicity and biochemical outcome in
772 patients. *Int J Radiat Oncol Biol Phys* **53** 1111-6

[37] Nutting C, Dearnaley D P and Webb S 2000 Intensity modulated radiation therapy: a clinical review. *Br J Radiol* **73** 459-69

[38] Xia P, Pickett B, Vigneault E, Verhey L J and Roach M, III 2001 Forward or inversely planned segmental multileaf collimator IMRT and sequential tomotherapy to treat multiple dominant intraprostatic lesions of prostate cancer to 90 Gy. *Int J Radiat Oncol Biol Phys* **51** 244-54

[39] Grigorov G, Kron T, Wong E, Chen J, Sollazzo J and Rodrigues G 2003 Optimization of helical tomotherapy treatment plans for prostate cancer. *Phys Med Biol* **48** 1933-43

[40] Cheng J C, Chao K S and Low D 2001 Comparison of intensity modulated radiation therapy (IMRT) treatment techniques for nasopharyngeal carcinoma. *Int J Cancer* **96** 126-31

[41] Ozyigit G and Chao K S 2002 Clinical experience of head-and-neck cancer IMRT with serial tomotherapy. *Med Dosim* **27** 91-8

[42] Lee N, Xia P, Quivey J M, Sultanem K, Poon I, Akazawa C et al. 2002 Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience. *Int J Radiat Oncol Biol Phys* **53** 12-22

[43] Fiorino C, Dell'Oca I, Pierelli A, Broggi S, De Martin E, Di Muzio N et al. 2006 Significant improvement in normal tissue sparing and target coverage for head and neck cancer by means of helical tomotherapy. *Radiother Oncol* **78** 276-82

[44] Fuss M, Salter B J, Sadeghi A, Vollmer D G, Hevezi J M and Herman T S 2002 Fractionated stereotactic intensity-modulated radiotherapy (FS-IMRT) for small acoustic neuromas. *Med Dosim* **27** 147-54

[45] Meeks S L, Buatti J M, Bova F J, Friedman W A, Mendenhall W M and Zlotecki R A 1998 Potential clinical efficacy of intensity-modulated conformal therapy. *Int J Radiat Oncol Biol Phys* **40** 483-95

[46] Lattanzi J, McNeely S, Pinover W, Horwitz E, Das I, Schultheiss T E et al. 1999 A comparison of daily CT localization to a daily ultrasound-based system in prostate cancer. *Int J Radiat Oncol Biol Phys* **43** 719-25

[47] Tomé W A, Meeks S L, McNutt T R, Buatti J M, Bova F J, Friedman W A et al. 2001 Optically guided intensity modulated radiotherapy. *Radiother Oncol* **61** 33-44

[48] Low D A, Grigsby P W, Dempsey J F, Mutic S, Williamson J F, Markman J et al. 2002 Applicator-guided intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys* **52** 1400-6

[49] Mutic S, Dempsey J F, Bosch W R, Low D A, Drzymala R E, Chao K S C et al. 2001 Multimodality image registration quality assurance for conformal three-dimensional treatment planning. *Int J Radiat Oncol Biol Phys* **51** 255-60

[50] Jaffray D A and Siewertsen J H 2000 Cone-beam computed tomography with a flat-panel imager: initial performance characterization. *Med Phys* **27** 1311-23

[51] Jaffray D A, Siewertsen J H, Wong J W and Martinez A A 2002 Flat-panel cone-beam computed tomography for image-guided radiation therapy. *Int J Radiat Oncol Biol Phys* **53** 1337-49

[52] Wong J R, Grimm L, Uematsu M, Oren R, Cheng C W, Merrick S et al. 2005 Image-guided radiotherapy for prostate cancer by CT-linear accelerator combination: prostate movements and dosimetric considerations. *Int J Radiat Oncol Biol Phys* **61** 561-9

[53] Mackie T R, Kapatoes J, Ruchala K, Lu W, Wu C, Olivera G et al. 2003 Image guidance for precise conformal radiotherapy. *Int J Radiat Oncol Biol Phys* **56** 89-105

[54] Ramsey C R, Langen K M, Kupelian P A, Scaperoth D D, Meeks S L, Mahan S L et al. 2006 A technique for adaptive image-guided helical tomotherapy for lung cancer. *Int J Radiat Oncol Biol Phys* **64** 1237-44

[55] Hoogeman M S, van Herk M, de Bois J and Lebesque J V 2005 Strategies to reduce the systematic error due to tumor and rectum motion in radiotherapy of prostate cancer. *Radiother Oncol* **74** 177-85
[56] Smitsmans M H, Wolthaus J W, Artignan X, de Bois J, Jaffray D A, Lebesque J V et al. 2004 Automatic localization of the prostate for on-line or off-line image-guided radiotherapy. *Int J Radiat Oncol Biol Phys* 60 623-35

[57] Yan D, Vicini F, Wong J and Martinez A 1997 Adaptive radiation therapy. *Phys Med Biol* 42 123-32

[58] Lof J, Lind B K and Brahme A 1998 An adaptive control algorithm for optimization of intensity modulated radiotherapy considering uncertainties in beam profiles, patient set-up and internal organ motion. *Phys Med Biol* 43 1605-28

[59] Martinez A A, Yan D, Lockman D, Brabbins D, Kota K, Sharpe M et al. 2001 Improvement in dose escalation using the process of adaptive radiotherapy combined with three-dimensional conformal or intensity-modulated beams for prostate cancer. *Int J Radiat Oncol Biol Phys* 50 1226-34

[60] Kapatoes J M, Olivera G H, Ruchala K J, Smilowitz J B, Reckwerdt P J and Mackie T R 2001 A feasible method for clinical delivery verification and dose reconstruction in tomotherapy. *Med Phys* 28 528-42

[61] Jiang S B 2006 Technical aspects of image-guided respiration-gated radiation therapy. *Med Dosim* 31 141-51

[62] Ramsey C R, Scaperoth D, Arwood D and Oliver A L 1999 Clinical efficacy of respiratory gated conformal radiation therapy. *Med Dosim* 24 115-9

[63] Keall P J, Kini V R, Vedam S S and Mohan R 2001 Motion adaptive x-ray therapy: a feasibility study. *Phys Med Biol* 46 1-10

[64] Keall P J, Joshi S, Vedam S S, Siebers J V, Kini V R and Mohan R 2005 Four-dimensional radiotherapy planning for DMLC-based respiratory motion tracking. *Med Phys* 32 942-51

[65] Vedam S S, Keall P J, Docef A, Todor D A, Kini V R and Mohan R 2004 Predicting respiratory motion for four-dimensional radiotherapy. *Med Phys* 31 2274-83

[66] Arnfield M R, Wu Q, Tong S and Mohan R 2001 Dosimetric validation for multileaf collimator-based intensity-modulated radiotherapy: a review. *Med Dosim* 26 179-88

[67] Kron T 2001 Radiation therapy requirements: what do we expect from gel dosimetry in *Proc. 2nd International Workshop on Radiation Therapy Gel dosimetry* Baldock C, De Deene, ed. (Queen'sland University of Technology, Brisbane, Australia) 2-9

[68] Galvin J M, Chen X G and Smith R M 1993 Combining multileaf fields to modulate fluence distributions. *Int J Radiat Oncol Biol Phys* 27 697-705

[69] Cadman P, Bassalow R, Sidhu N P, Ibbott G and Nelson A 2002 Dosimetric considerations for validation of a sequential IMRT process with a commercial treatment planning system. *Phys Med Biol* 47 3001-10

[70] Low D A, Mutic S, Dempsey J F, Gerber R L, Bosch W R, Perez C A et al. 1998 Quantitative dosimetric verification of an IMRT planning and delivery system. *Radiother Oncol* 49 305-16

[71] Van Esch A, Bohsung J, Sorvari P, Tenhunen M, Pajuusco M, Iori M et al. 2002 Acceptance tests and quality control (QC) procedures for the clinical implementation of intensity modulated radiotherapy (IMRT) using inverse planning and the sliding window technique: experience from five radiotherapy departments. *Radiother Oncol* 65 53-70

[72] Ting J Y and Davis L W 2001 Dose verification for patients undergoing IMRT. *Med Dosim* 26 205-13

[73] Archambault L, Arsenault J, Gingras L, Beddar A S, Roy R and Beaulieu L 2005 Plastic scintillation dosimetry: optimal selection of scintillating fibers and scintillators. *Med Phys* 32 2271-8

[74] Chuang C F, Verhey L J and Xia P 2002 Investigation of the use of MOSFET for clinical IMRT dosimetric verification. *Med Phys* 29 1109-15

[75] Engstrom P E, Haraldsson P, Landberg T, Sand H H, Aage E S and Nystrom H 2005 In vivo dose verification of IMRT treated head and neck cancer patients. *Acta Oncol* 44 572-8
Jursinic P A and Nelms B E 2003 A 2-D diode array and analysis software for verification of intensity modulated radiation therapy delivery. Med Phys 30 870-9

Letourneau D, Gulam M, Yan D, Oldham M and Wong J W 2004 Evaluation of a 2D diode array for IMRT quality assurance. Radiother Oncol 70 199-206

Poppe B, Blechschmidt A, Djouguela A, Kollhoff R, Rubach A, Willborn K C et al. 2006 Two-dimensional ionization chamber arrays for IMRT plan verification. Med Phys 33 1005-15

Wiezorek T, Banz N, Schwedas M, Scheithauer M, Salz H, Georg D et al. 2005 Dosimetric quality assurance for intensity-modulated radiotherapy feasibility study for a filmless approach. Strahlenther Onkol 181 468-74

Petric M P, Robar J L and Clark B G 2006 Development and characterization of a tissue equivalent plastic scintillator based dosimetry system. Med Phys 33 96-105

Partridge M, Ebert M and Hesse B M 2002 IMRT verification by three-dimensional dose reconstruction from portal beam measurements. Med Phys 29 1847-58

Van Esch A, Vanstraalen B, Verstraete J, Kutcher G and Huyskens D 2001 Pre-treatment dosimetric verification by means of a liquid-filled electronic portal imaging device during dynamic delivery of intensity modulated treatment fields. Radiother Oncol 60 181-90

Van Esch A, Depuydt T and Huyskens D P 2004 The use of an aSi-based EPID for routine absolute dosimetric pre-treatment verification of dynamic IMRT fields. Radiother Oncol 71 223-34

Warkentin B, Steciw S, Rathee S and Fallone B G 2003 Dosimetric IMRT verification with a flat-panel EPID. Med Phys 30 3143-55

Burman C, Chui C S, Kutcher G, Leibel S, Zelefsky M, LoSasso T et al. 1997 Planning, delivery, and quality assurance of intensity-modulated radiotherapy using dynamic multileaf collimator: a strategy for large-scale implementation for the treatment of carcinoma of the prostate. Int J Radiat Oncol Biol Phys 39 863-73

De Wagter C 2004 The ideal dosimeter for intensity modulated radiation therapy (IMRT): What is required? Journal of Physics: Conference Series 3 4-8

MacKenzie M A, Lachaine M, Murray B, Fallone B G, Robinson D and Field G C 2002 Dosimetric verification of inverse planned step and shoot multileaf collimator fields from a commercial treatment planning system. J Appl Clin Med Phys 3 97-109

Bogner L, Scherer J, Treutwein M, Hartmann M, Gum F and Amedick A 2004 Verification of IMRT: techniques and problems. Strahlenther Onkol 180 340-50

Kapatoes J M, Oliveira G H, Balog J P, Keller H, Reckwerdt P J and Mackie T R 2001 On the accuracy and effectiveness of dose reconstruction for tomotherapy. Phys Med Biol 46 943-66

Harms W B, Sr., Low D A, Wong J W and Purdy J A 1998 A software tool for the quantitative evaluation of 3D dose calculation algorithms. Med Phys 25 1830-6

Low D A, Harms W B, Mutic S and Purdy J A 1998 A technique for the quantitative evaluation of dose distributions. Med Phys 25 656-61

Mah E, Antolak J A, Scrirnger J W and Battista J 1989 Experimental evaluation of a 2D and 3D electron pencil beam algorithm. Phys Med Biol 34 1179-94

Van Dyk J, Barnett R B, Cygler J E and Shragge P C 1993 Commissioning and quality assurance of treatment planning computers. Int J Radiat Oncol Biol Phys 26 261-73

Low D A and Dempsey J F 2003 Evaluation of the gamma dose distribution comparison method. Med Phys 30 2455-64

Bakai A, Alber M and Nusslin F 2003 A revision of the gamma-evaluation concept for the comparison of dose distributions. Phys Med Biol 48 3543-53

Depuydt T, Van Esch A and Huyskens D P 2002 A quantitative evaluation of IMRT dose distributions: refinement and clinical assessment of the gamma evaluation. Radiother Oncol 62 309-19

Fraass B, Doppke K, Hunt M, Kutcher G, Starkschall G, Stern R et al. 1998 American
Association of Physicists in Medicine Radiation Therapy Committee Task Group 53: quality assurance for clinical radiotherapy treatment planning. *Med Phys* **25** 1773-829

[98] Islam K T, Dempsey J F, Ranade M K, Maryanski M J and Low D A 2003 Initial evaluation of commercial optical CT-based 3D gel dosimeter. *Medical Physics* **30** 2159-68

[99] Kipouros P, Papagiannis P, Sakellion L, Karaisskos P, Sandilos P, Baras P et al. 2003 3D dose verification in Ir-192 HDR prostate monotherapy using polymer gels and MRI. *Med Phys* **30** 2031-9

[100] Vergote K, De Deene Y, Duthoy W, De Gersem W, De Neve W, Achten E et al. 2004 Validation and application of polymer gel dosimetry for the dose verification of an intensity-modulated arc therapy (IMAT) treatment. *Phys Med Biol* **49** 287-305

[101] Sandilos P, Angelopoulos A, Baras P, Dardoufas K, Karaisskos P, Kipouros P et al. 2004 Dose verification in clinical IMRT prostate incidents. *International Journal of Radiation Oncology, Biology, Physics* **59(5):1540-7,

[102] Childress N L, White R A, Bloch C, Salehpour M, Dong L and Rosen I I 2005 Retrospective analysis of 2D patient-specific IMRT verifications. *Med Phys* **32** 838-50

[103] Ling C C, Humm J, Larson S, Amols H, Fuks Z, Leibel S et al. 2000 Towards multidimensional radiotherapy (MD-CRT): biological imaging and biological conformality. *Int J Radiat Oncol Biol Phys* **47** 551-60

[104] Keall P and Baldock C 1999 A theoretical study of the radiological properties and water equivalence of Fricke and polymer gels used for radiation dosimetry. *Australas Phys Eng Sci Med* **22** 85-91

[105] Gore J C, Kang Y S and Schulz R J 1984 Measurement of radiation dose distributions by nuclear magnetic resonance (NMR) imaging. *Phys Med Biol* **29** 1189-97

[106] Maryanski M J, Gore J C, Kennan R P and Schulz R J 1993 NMR relaxation enhancement in gels polymerized and cross-linked by ionizing radiation: a new approach to 3D dosimetry by MRI. *Magn Reson Imaging* **11** 253-8

[107] Schreiner L J. Gel Dosimetry: Motivation and Historical Foundation. 1999 In *Proc. 1st International Workshop on Radiation Therapy Gel dosimetry*. Schreiner L J, Audet C, ed. (Canadian Organization of Medical Physicists Edmonton) 1-10.