

Introduction of Image Guided Radiotherapy into Clinical Practice



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INTRODUCTION OF IMAGE GUIDED RADIOTHERAPY INTO CLINICAL PRACTICE

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FOREWORD

Radiotherapy is an essential component in the treatment management of cancer patients, either alone or in combination with surgery or chemotherapy, and for both cure and palliation. Imaging the patient has always been part of safe and effective radiotherapy, and recent advances in technology have allowed frequent imaging of the patient in the treatment room in the treatment position at the time of treatment. This process of in-room imaging and its associated actions are referred to in the radiotherapy community as image guided radiotherapy (IGRT).

In external beam radiotherapy, intensity modulated radiotherapy (IMRT) has been introduced in many radiotherapy departments, but there is a recognition that IMRT without some form of in-room image guidance can lead to compromised treatment. Technological advances have meant that verification of the positioning of the patient has progressed from radiographic film analysed after treatment (off-line) to advanced imaging of the patient volume at the time of treatment with immediate on-line corrective strategies as part of IGRT. Three dimensional conformal radiotherapy (3-D CRT) or IMRT with IGRT requires more technology, equipment, staff and training resources. Advanced IGRT with motion management and treatment gating requires even more investment in resources.

The IAEA has received a number of requests for guidance from radiotherapy departments that wish to upgrade their facilities to IGRT through the technical cooperation programme. These requests are expected to increase in the near future. Since the introduction of image guidance technology is complex, there is a recognition that departments need guidance on the preparation, resources and commissioning processes involved. In addition, the current status of the evidence supporting the use of IGRT in terms of patient outcomes has to be considered when planning to invest in these technologies.

To respond to the need of Member States to establish guidelines for the introduction of IGRT into clinical practice, a consultants meeting was convened to discuss the necessary steps and the milestones for the transition to IGRT. The recommendations made by the international experts and described here supplement IAEA publications on setting up a radiotherapy programme and making the transition to 3-D CRT and IMRT. Taken together, the publications provide a comprehensive overview of the required radiotherapy infrastructure and processes for a broad spectrum of radiotherapy services.

This publication is addressed to those professionals and administrators involved in the development, implementation and management of radiotherapy programmes who seek to improve their practice by incorporating imaging with the explicit aim of achieving reduced uncertainties and increased accuracy. The publication provides guidelines for the introduction of IGRT and highlights the milestones to be reached by radiotherapy departments. These guidelines and milestones facilitate the process and represent the continuation of the work being undertaken by the IAEA to provide access to safer and higher quality treatment for the steadily increasing number of cancer patients in Member States.

The IAEA officer responsible for this publication was B. Healy of the Division of Human Health.

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1. INTRODUCTION

1.1. BACKGROUND

Although there is no uniformly accepted definition as to where conventional verification imaging ends and image guided radiotherapy (IGRT) begins, there is general agreement that the key features are as follows [1]:

- (a) The availability of high quality imaging equipment in the treatment room.
- (b) The ability to visualize key anatomical structures, including the target, with the patient in the treatment position, with the main objective being to inform beam placement. Appropriate surrogates may be used to infer the positions of organs relative to each other.
- (c) A protocol to act on the findings. This could be done on-line (i.e. prior to turning on the radiation beam) or off-line between fractions.

For the purposes of this publication, the complexity of IGRT is captured by a number of levels (see Table 1). The transition from Level 1 to Level 2 is the main focus of this publication. Level 3 is an advanced level with significantly increased complexity and it is beyond the scope of this publication to describe it in full.

In this publication, Level 1 is the level of radiotherapy necessary before embarking on an IGRT programme. Three dimensional conformal radiotherapy (3-D CRT) is the basis of this level, with dose prescribing, reporting and recording as recommended by the International Commission on Radiation Units and Measurements (ICRU) [2]. Level 1 involves the off-line review of megavoltage (MV) portal images with an electronic portal imaging device (EPID) or radiographic film. The portal images include beam's eye views or orthogonal images. Level 1 in this publication corresponds to Level 2 3-D CRT in Ref. [5].

Level 2 expands to include paired orthogonal kilovoltage (kV) imaging and volumetric imaging, with associated off-line or on-line IGRT protocols as appropriate. Fiducial markers may also be used. For Level 2, a linear accelerator with a multileaf collimator, EPID and a kV imaging system is required. Analysis of patient shifts and action levels is recommended in Level 2. Level 3 progresses to include respiratory motion management (e.g. gated treatment, 4-D planning and verification imaging), intrafraction target visualization and 6-D correction of the treatment. Meta-analysis of the aggregated patient population data is required, and options for class based plan adaptation should be considered.

1.2. OBJECTIVE

This publication covers various aspects of the introduction of IGRT, including clinical evidence, resources, milestones, a description of clinical processes, education, training and staffing requirements, and quality assurance guidelines.

1.3. SCOPE

This publication applies to Member States that use 3-D CRT or intensity modulated radiotherapy (IMRT). Its main focus is on the transition from off-line portal imaging to kV X ray volumetric and planar imaging for patient positioning at the time of external beam radiotherapy (EBRT). It is assumed that the basis in most departments is 3-D CRT, since the implementation of IGRT is considered a prerequisite for IMRT. This publication is concerned with X ray based EBRT and not brachytherapy, where there are different issues for patient positioning relative to the radiation source. While the publication concentrates on kV X ray imaging for IGRT, it is acknowledged that there are numerous complementary solutions for imaging the patient at the time of treatment (e.g. ultrasound, magnetic resonance and beacon transponders). The principles set out in this publication may also be applied to the introduction of these technologies into clinical practice.

Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

Procedure	Level 1 3-D CRT, including off-line portal imaging	Level 2 Standard IGRT: 3-D CRT/IMRT with off-line or on-line IGRT	Level 3 Advanced IGRT: 3-D CRT/IMRT with on-line advanced IGRT	
Patient data acquisition; target and organs at risk definition				
Implanted fiducial markers	Optional	As appropriate for target imaging	As appropriate for target imaging	
Immobilization	Customized to the patient	Same as Level 1	Customized, including motion management	
Imaging methodology	CT imaging without contrast agents, with or without fusion to contrast CT, MR, PET, etc.	Same as Level 1	Same as Level 1 plus 4-D capability	
Organs at risk definition	Volume based	Same as Level 1	Same as Level 1	
Target definition	Volume based	Same as Level 1	Customized ITV included	
Margins	Literature/local data	Same as Level 1	Informed by local data	
Treatment planning				
Plan optimization	Forward planning with 3-D TPS and customized blocking and/or MLC	Forward planning (3-D CRT) or inverse planning (IMRT) with MLC	Same as Level 2 plus 4-D as appropriate	
Plan evaluation	Isodose lines, DVHs and dose constraints	Same as Level 1 Peer review recommended	Same as Level 1 Peer review	
Dose reporting	ICRU Reports 50 [2] and 62 [3]	ICRU Reports 50 [2], 62 [3] and 83 [4]	ICRU Reports 50 [2], 62 [3] and 83 [4]	
Treatment delivery				
Treatment delivery unit	MV EBRT unit with MLC (desirable) or customized blocks	MV linear accelerator with MLC, EPID and volumetric imaging capability	Same as Level 2 plus motion management and 6-D corrections	
Initial patient positioning	Move from anatomical reference	Same as Level 1	Same as Level 1 with consideration of motion management	
Verification reference image	DRR	DRR or planning CT dataset	Same as Level 2 plus 4-D reference image	
Verification image	MV portal images with EPID or radiographic film	Same as Level 1 plus volumetric images or paired orthogonal kV images	Same as Level 2 plus 4-D volumetric image	
Verification strategy	Review off-line	Off-line or on-line IGRT protocol	On-line with options for adaptation of treatment plan	
Record and verify system with image review capability	Desirable	Mandatory, including automated analysis of patient shifts in order to assess action levels	Mandatory, including tools for meta-analysis of patient shifts to refine class based adaptive strategies	
Follow-up evaluation	Essential	Essential	Essential	

TABLE 1. LEVELS OF IGRT ACCORDING TO THE METHODOLOGY AND TOOLS ASSOCIATED WITH EACH STEP OF THE PROCEDURE

Note: 3-D CRT — three dimensional conformal radiotherapy; CT — computed tomography; DRR — digitally reconstructed radiograph; DVH — dose volume histogram; EBRT — external beam radiotherapy; EPID — electronic portal imaging device; ICRU — International Commission on Radiation Units and Measurements; IGRT — image guided radiotherapy; IMRT — intensity modulated radiotherapy; ITV — internal target volume; kV — kilovoltage; MLC — multileaf collimator; MR — magnetic resonance; MV — megavoltage; PET — positron emission tomography; TPS — treatment planning system.

1.4. STRUCTURE

Section 2 provides a brief overview of the clinical evidence for IGRT. Section 3 describes IGRT technology and treatment correction. Section 4 explores how an IGRT programme can be established and the equipment and protocols required. Section 5 lays out the roles and responsibilities of IGRT staff and the necessary training. Section 6 concludes with IGRT in clinical practice, including an outline of the milestones and a description of quality assurance, uncertainties, planning margins, and justification and optimization. Appendix I is a self-evaluation questionnaire to determine the state of readiness of an institution to transition to IGRT. Appendix II provides an example calculation of a clinical target volume (CTV) to planning target volume (PTV) margin.

2. CLINICAL EVIDENCE FOR IMAGE GUIDED RADIOTHERAPY

In conventional radiotherapy, set-up uncertainties are reduced through patient immobilization, and internal motion is estimated based on the study of analogous patient populations. Imaging using the treatment beam enables identification of gross misalignment. However, the target is not always visible on portal images, and the identifiable surrounding anatomy is often a poor surrogate for the target. In this sense, the internal motion of thoracic, abdominal and pelvic organs, independent of the bony anatomy, has been well demonstrated. It is also well documented that target motion varies from patient to patient and from day to day.

Since the 1990s, significant technological advances have resulted in the use of more advanced imaging at the time of treatment delivery. It stands to reason that better target visualization at the time of treatment can either lead to more consistent targeting with the same PTV margins or maintain the same likelihood of appropriate target dosing with a smaller margin.

Although CTV to PTV margin reduction has been the principal focus of IGRT implementation and research [6–9], the acquisition of serial volumetric images holds the promise of other improvements in the radiotherapy process. As patient anatomy changes over time, IGRT images should help to identify patients for whom the treatment plan must be adapted. In certain cases, such as variations in patient weight or bladder volume, the barriers to frequent adaptation are logistical or technical. In other cases, the barrier is an imperfect understanding of tumour regression — what dose should be delivered to tissue where the tumour is no longer visible on imaging? In addition to better targeting and adaptation, IGRT may offer other insights, such as prognostication — do patients with faster responding tumours have a better outcome?

In most cases, IGRT has led to the evolution of current treatment paradigms (i.e. the reduction of margins). Sometimes IGRT has been more disruptive, as in the case of hypofractionated ablative radiotherapy or 'frameless' cranial radiosurgery.

The improvements in accuracy and precision achieved with IGRT have been well documented based on phantom and patient studies [10–13]. As with many technical advances in radiotherapy, the clinical benefits have not been as well documented, since some of the reductions expected in late toxicities will only be observed years after the radiotherapy was administered. No randomized trial has isolated IGRT as the experimental variable, and it is unlikely that such a trial will be performed. Retrospective review pre- and post-IGRT implementation in prostate and head and neck radiotherapy has documented significant reductions in toxicity (e.g. rectal bleeding and oesophageal stricture) [14–16]. In many other disease sites, toxicity correlates well with irradiated volume, and clinically significant reductions in toxicity can reasonably be expected through the use of IGRT.

A key aspect of IGRT is the ability to generate data on set-up, organ motion and deformation for individual patients and groups of patients. In addition to the impact on margins, IGRT can identify trends in patients (e.g. reduced rectal filling towards the end of treatment) and equipment (e.g. small couch sag) that are too small to notice in individual treatment courses, but can still result in improvements to treatment processes. As such, the data generated through frequent imaging constitute an important learning opportunity.

As the practice of IGRT with X rays and MV imaging systems involves an additional dose burden to the patient [17], justification for the medical exposure is required. Paragraph 3.155 of IAEA Safety Standards Series

No. GSR Part 3, Radiation Protection and Safety of Radiation Sources: International Basic Safety Standards [18], states that "medical exposures shall be justified by weighing the diagnostic or therapeutic benefits...that they are expected to yield against the radiation detriment that they might cause" and:

"3.157. The justification of medical exposure for an individual patient shall be carried out by means of consultation between the radiological medical practitioner and the referring medical practitioner, as appropriate".

The radiation oncologist needs to prescribe the IGRT (including the type and frequency of imaging), balancing the clinical evidence of the benefits of IGRT against the expected dose to the patient from the IGRT procedures, as advised by the medical physicist. Furthermore, the benefits of IGRT need to be balanced against the costs, added time and general increase in treatment complexity. For most clinical scenarios, the benefits are felt to outweigh the costs. This balance should continue to improve with advances in the image quality, the speed of the IGRT process and the reduction or elimination of the imaging dose.

3. TECHNOLOGY OF IMAGE GUIDED RADIOTHERAPY

3.1. IMAGING

The definition of IGRT used in this publication involves the application of imaging for the verification of radiotherapy treatments [1, 19–21]. Some uses of advanced imaging for treatment planning, such as functional imaging for dose painting have, at times, also been referred to as IGRT [22]. These are not the focus of this publication.

3.1.1. Cone-beam computed tomography systems

The imaging technology most commonly used for IGRT verification is the kV cone-beam computed tomography (kV-CBCT) system [23]. This is most often in addition to an EPID, which enables planar imaging of the treatment beam. In the most common implementation of kV-CBCT, a kV X ray tube and flat panel imager are mounted on the treatment machine gantry at 90 degrees to the treatment beam. At the start of treatment, the patient is positioned on the treatment couch and the gantry is rotated around the patient to acquire the projection data to enable CBCT reconstruction. The kV-CBCT system is provided with a pre-set range of imaging protocols. These specify quantities such as the range of gantry angles to acquire the scan data, the position of the flat panel, the size of the kV X ray beam and any filters used to vary the intensity profile of the X ray beam (e.g. a bow-tie filter). Volumetric X ray systems typically acquire scans over several seconds or even minutes. This publication will mainly use this type of system as the basic model to describe IGRT. The best practices described, however, are transferrable to other IGRT technologies.

MV-CBCT [24] involves using the MV treatment source to acquire the cone-beam scan. Thus, it dispenses with the extra X ray source and imaging panel, but is in many other respects essentially equivalent to kV-CBCT.

3.1.2. Fan-beam computed tomography systems

Helical tomotherapy devices [25] use an MV fan beam for treatment, known as megavoltage computed tomography (MVCT). The patient is passed through the isocentre of the system as the fan beam rotates and the beam profile is varied to deliver the treatment with the same geometry as a helical computed tomography (CT) scan. For imaging, the beam may be rotated without intensity variation, and an array of detectors is used to image the radiation intensity transmitted through the patient.

3.1.3. Planar imaging systems

The kV-CBCT system flat panels are not only used to produce orthogonal planar projections, but can also be used for fluoroscopy, and they can often complement 3-D and 4-D images. Of course, the EPID can be used for IGRT in certain situations where image quality is not a limiting factor. For example, orthogonal EPID images can be acquired prior to prostate cancer radiotherapy and set-up corrections made on the basis of bony anatomy or implanted radio-opaque fiducials [26].

Another class of system employs room mounted, fixed kV X ray units coupled to flat panel imagers. Typically, two X ray units are used to image the target from different directions. This allows triangulation to define the target position in 3-D [19, 27]. Implanted fiducial markers, bony anatomy or, less commonly, direct tumour visualization are used with such systems to enable accurate 3-D location of the treatment target. Multiple images may be acquired during the respiratory cycle to enable the 4-D capability of Level 3 IGRT [28]. Examples of such systems include ExacTrac [29], Cyberknife [30] and Vero [31]. The dose to the patient would be substantial if imaging were performed continuously throughout a typical treatment fraction; hence, these devices are often pulsed and used in conjunction with a non-ionizing system.

3.1.4. Non-ionizing visualization systems

Volumetric ultrasound has been demonstrated to be useful for soft tissue targeting throughout the body, but its most reliable application has been in imaging the prostate [32]. With a transperineal probe, intrafraction pelvic imaging is now possible. Magnetic resonance imaging (MRI) based IGRT has recently been introduced to the clinic. It offers the promise of detailed soft tissue visualization before and during treatment. The challenges of combining MRI with linear accelerator systems are significant, and these systems, whether based on cobalt [33] or linear accelerators [34], will entail significant additional costs and complexity.

Fiducial marker systems that are not based on X rays are becoming more readily available. These can use electromagnetic transponders and a radio frequency system to measure transponder positions. When they are implanted in the target, the transponders can provide direct feedback on tumour position or they can be used to track a surrogate to the target, such as the chest wall [35].

A range of optical imaging systems are available for IGRT. One of the first was the Varian Real-Time Position Monitor [36], which measures breathing phases. Other systems involve detailed measurement of the patient surface using reflections of light projected onto the patient surface. Another example of an optical imaging system is Vision RT [37]. These types of system are generally used in conjunction with the radiological imaging systems discussed above to enable the position of the internal anatomy to be inferred from the outline image [38, 39]. An example is the Cyberknife system, which combines infrared marker tracking with kV X ray triangulation [30].

3.2. TREATMENT CORRECTION

The first stage of treatment correction is to compare the measured patient position with that in the treatment plan, using a reference image and image registration tools that can be translated into set-up corrections.

For the correction of basic set-up displacements, a remotely controllable treatment couch reduces the risk of errors from carrying out the correction manually and reduces the time needed for the intervention. The 6-D treatment couch [40, 41] enables the correction of both translations and rotations in the three spatial planes. An alternative to patient position adjustment is to change the treatment beam position. This can involve modifying the start angle on a helical tomotherapy unit, the robot position on a robotic radiosurgery unit or the angle of the gimbal on a gimballed treatment unit [42].

For the correction of more complex patient changes, deformable registration of treatment and reference images may be necessary. This requires a computer algorithm to match the images using a set of 'goodness of match' criteria [43]. A decision should then be made as to whether the patient set-up or treatment can be altered in response to the change, or if replanning is needed to adapt the treatment.

A range of solutions have been developed for motion management based on imaging. Detailed discussion of, and recommendations for motion management, are beyond the scope of this publication. Approaches include the following:

- (a) Generating a plan that is optimized for the motion profile [44];
- (b) Controlling the patient's breathing, for example through voluntary holding of the breath [45] and active breathing coordination [46];
- (c) Gating the beam to only deliver radiation during part of the breathing cycle [47];
- (d) Tracking the beam to follow the motion [42, 48, 49].

4. IMAGE GUIDED RADIOTHERAPY PROGRAMME

4.1. ESTABLISHING THE PROGRAMME

Starting an IGRT programme requires considerable planning. There are significant differences between Level 1 off-line portal imaging and Levels 2 and 3 in terms of equipment, imaging, treatment planning, image handling and review, and database analysis and management (see Table 1, in Section 1). The logistical steps necessary to establish an IGRT programme include the following:

- (a) Appoint an IGRT implementation committee;
- (b) Define the scope of the programme, including preparing a structured timeline;
- (c) Identify the necessary equipment, including software;
- (d) Determine the possible impact on patient throughput;
- (e) Develop a programme budget, perform market research of IGRT equipment and purchase equipment;
- (f) Develop staffing needs for the programme and hire new staff;
- (g) Allow a reasonable timeline to perform installation, acceptance testing and commissioning;
- (h) Train all personnel involved in the programme;
- (i) Develop the necessary guidelines, policies and procedures;
- (j) Develop and implement a comprehensive quality assurance programme for IGRT.

It is important to allow sufficient time for training prior to the arrival of the equipment so that trained medical physicists are in place to carry out acceptance testing and commissioning. Radiation oncologists and radiation therapists (also known as radiation therapy technologist, RTTs) also require relevant training during, or prior to, the commissioning phase. The equipment resources required to establish such a programme are outlined in this section and human resources is covered in Section 5. An estimated timeline for the introduction of IGRT is given in Table 2.

4.1.1. Imaging for planning

Volumetric imaging for treatment planning is a prerequisite for IGRT and this is usually achieved with CT (see Ref. [5] for a description of the simulation process for 3-D CRT and IMRT).

4.1.2. Immobilization equipment

Immobilization equipment is a prerequisite for some treatment sites. Because of the nature of CRT/IMRT treatment, reproducible immobilization techniques are essential to use this treatment technique safely. If the reproducibility that can be achieved with the immobilization system is not already known, it will be necessary to study it. It is important to verify that immobilization equipment is compatible with in-room imaging equipment to avoid collisions and interference when generating the image.

Process	Duration	Responsibility
Appoint and convene an IGRT implementation committee	1 week	Management
Define the scope of the programme	1 month	IGRT committee
Identify the necessary equipment, including software	1 month	IGRT committee
Define the possible impact on patient throughput	1 week	IGRT committee
Purchase equipment	3–6 months	Management
Hire new staff	6 months	Management
Installation, acceptance testing and commissioning	1 month	Manufacturer and medical physicist
Train personnel	3 months	Management and IGRT committee
Develop guidelines, policies and procedures	3 months	IGRT committee
Develop quality assurance programme	1 month	Medical physicist and radiation therapist

TABLE 2. TIMETABLE FOR THE INTRODUCTION OF IMAGE GUIDED RADIOTHERAPY

4.1.3. 3-D treatment planning system

For IGRT, the treatment planning system needs to be capable of generating reference images (e.g. digitally reconstructed radiographs and CT planning image sets). It is highly desirable that the treatment planning system is able to attach structures or isodose lines to the reference image. The coordinates and scale need to be included in the reference image.

4.1.4. Treatment unit

A linear accelerator fitted with a multileaf collimator is required for the delivery of planned CRT/IMRT with IGRT. The linear accelerator will also be fitted with an EPID, which can be used for the generation of beam portals and for quality assurance. The EPID has traditionally been used for patient set-up verification, but has now been complemented by kV planar and volumetric imaging systems. It is desirable that couch translations can be initiated and performed from the treatment console.

It is noted that specialized treatment units such as robotic systems, gimballed linear accelerators, helical tomotherapy units and units with room mounted X ray systems also include image guidance tools. It would also be feasible to add an X ray IGRT system to a ⁶⁰Co teletherapy machine, but this is not currently commercially available.

4.1.5. Record and verify system and network system

A record and verify system (RVS) is needed to ensure, at a minimum, that the planned CRT/IMRT is delivered as prescribed and that the appropriate reference images are available at the treatment unit. Care needs to be taken to ensure that errors do not occur during the transfer of data between treatment planning systems, simulators and treatment machines [50, 51]. An electronic network system for data transfer from imaging facilities to the treatment planning system and then to the delivery systems is required and this should comply with Digital Imaging and Communications in Medicine (DICOM) and DICOM-RT protocols. In many radiotherapy departments, a comprehensive oncology information system, such as MOSAIQ or Aria, manages the flow and storage of patient information, including IGRT images. Special attention should be given to the integration of the IGRT system into the RVS (in some commercial systems the IGRT RVS is not directly connected to the linear accelerator RVS,

allowing different patients or treatment courses to be selected on both systems). Where the IGRT system has not been integrated into the linear accelerator RVS, appropriate precautions should be taken to avoid erroneous patient identification.

4.1.6. Image review

The console in the linear accelerator control area must be capable of performing image registration and identifying positional differences between the reference image and the verification image. Quantitative results for the differences need to be displayed unambiguously and stored electronically for further analysis and processing. It is desirable that the required patient set-up corrections can be applied remotely, in which case an additional verification might be considered.

For the off-line review of verification images, a sufficient number of networked image review workstations with appropriate tools needs to be available. Consideration should be given to the export of the patient shift data for further analysis, including meta-analysis.

In planning IGRT, it needs to be recognized that there will be significant data storage requirements for IGRT images. Appropriate memory space will be required, in addition to established procedures for archiving and retrieval.

4.1.7. Quality assurance tools

Most radiotherapy departments are not equipped with tools for imaging system quality assurance. Access to image quality phantoms, specific dosimeters and expertise is required. Collaboration with a radiology department is often recommended where appropriate. Special attention should be given to geometric precision, as this is not usually part of conventional quality assurance for diagnostic imaging systems. Experts recommend the use of dedicated phantoms to verify the coincidence between the treatment and imaging isocentres.

4.1.8. Indicative costs

Table 3 contains a list of IGRT equipment and indicative cost. The table excludes the costs associated with additional data storage requirements or upgrades to the 3-D treatment planning system, treatment unit, record and verify system, and network system required for IMRT capability.

Equipment	Cost
Upgrade of linear accelerator to kV imaging	300 000
CBCT option for kV imaging system	100 000
Fiducial markers (set of three gold seeds)	100
Dosimetry test kit, including kVp and HVL test equipment	10 000
Geometric phantom with markers	3 000
Image quality phantom (planar imaging)	3 000
Image quality phantom (volumetric imaging)	10 000

TABLE 3. INDICATIVE COSTS OF EQUIPMENT FOR IMAGE GUIDED RADIOTHERAPY (US \$, 2016)

Note: CBCT — cone-beam computed tomography; HVL — half value layer; kV — kilovoltage; kVp — kilovolt peak.

4.1.9. Image guided radiotherapy protocols

IGRT protocols can be broadly divided into the categories off-line and on-line. The decision of which to use depends on the site being treated and departmental resources, including the need to balance treatment accuracy with workload and expertise.

In an off-line review, the deviations of previous fractions are considered and analysed, and this in turn helps to determine the set-up of subsequent fractions. Off-line protocols are efficient in the correction of systematic effects, which, if uncorrected, have been demonstrated to cause a shift in the cumulative dose distribution [52]. Off-line correction protocols are therefore most suitable when the ratio of random to systematic deviation is small. In on-line imaging, image acquisition and corrections of necessary shifts are performed before treatment delivery. Random deviations can only be corrected for with an on-line IGRT protocol.

4.1.9.1. Off-line IGRT protocols

There are two main categories of off-line correction protocol, the 'shrinking action level' (SAL) protocol, described by Bel et al. [53] in 1993, and the 'no action level' (NAL) protocol, first described by de Boer and Heijmen [54] in 2001 and further developed into the 'extended no action level' (e-NAL) in 2007 [55].

In the SAL protocol (see Fig.1), the average of the systematic uncertainty is measured. This is then compared to a predefined threshold or action level. If the average exceeds the threshold, then a correction is performed on subsequent fractions. The basis of this IGRT protocol is that the systematic effect should decrease with time, so



FIG. 1. Shrinking action level (SAL) off-line IGRT protocol.

the threshold or action level decreases accordingly for the remainder of the course by the inverse square root of the number of fractions. This is given by α/\sqrt{N} , where α is the initial action level and N is the number of fractions. N_{max} is the maximum number of subsequent fractions considered to be appropriate for a given clinical situation and this is what determines the final action level to be applied. No more corrections are applied once the set-up is consistently within tolerance.

The SAL protocol is useful because it avoids a set-up being corrected for prematurely (i.e. a deviation which could be random, not systematic). However, it requires a large number of imaged fractions that are not defined from the outset, thereby leading to unpredictable dose and imaging workload.

The basis of the NAL protocol is that the mean displacement yields the best estimate of the systematic effect after a number of treatment fractions. As seen in Fig. 2, the patient is imaged for a predefined number of fractions (n_m) . The mean measured displacement is then calculated. The measured correction is then applied to all subsequent fractions and no further image acquisition occurs.



FIG. 2. No action level (NAL) off-line IGRT protocol.



FIG. 3. Extended no action level (e-NAL) off-line IGRT protocol.

In the e-NAL protocol (see Fig. 3), the protocol is further expanded to include weekly imaging following the correction. This is to monitor any other systematic effects due to time trends or any other transitions.

The NAL IGRT protocol requires fewer images than the SAL. However, where the ratio of random to systematic set-up effects is larger, its ability to estimate the systematic set-up effects quickly is likely to be limited, and additional imaging will be required, or an on-line approach may be considered, depending on the clinical scenario.

4.1.9.2. On-line IGRT protocols

In on-line IGRT, action is taken immediately after imaging of the patient to determine the shift of the acquired image from the reference image [56]. In zero action level protocols, the shift is applied to the patient set-up irrespective of the size of the shift. This is by way of contrast to action level protocols, where shifts are only applied if they are larger than a predetermined action level (e.g. 2 mm) [9]. In either case, the shifts need to be recorded electronically and reviewed. The on-line protocol will specify the frequency of imaging, for example, if repeat imaging is conducted after shifts to confirm their efficacy. Finally, consideration should be given in the protocol to the actions required when the size of the shift is above a certain threshold, including the RTT re-entering the treatment room to check the patient set-up, removing the patient from the treatment couch to correct for patient related factors (e.g. bladder filling) or consulting with a radiation oncologist.

4.2. EXTERNAL BEAM RADIOTHERAPY WITH IMAGE GUIDED RADIOTHERAPY

The process for EBRT with IGRT is illustrated in Figs 4 and 5. Only those processes that are introduced or modified by the introduction of Level 2 IGRT are described in this section (see Ref. [5] for a general description of the 3-D CRT and IMRT processes).

4.2.1. Implantation of fiducial markers

Fiducial markers can be used with IGRT as a surrogate for soft tissue positioning. The benefits of fiducial markers include:

- (a) The ability to define the target position when soft tissue is difficult to visualize;
- (b) Target localization in cases where motion of the target is a concern;
- (c) The reduction of inter-observer variability in target positioning;
- (d) Increased patient throughput through quick identification of the fiducial marker position in images.

The implantation of fiducial markers varies, depending on the treatment site and the patient management stage. An appropriately trained health care professional is needed for the marker insertion procedure. Markers are often implanted with biopsy needles or at the time of surgery. The choice of marker depends on the imaging for treatment planning, IGRT and any further imaging required post-treatment. Consideration needs to be given to the possibility of marker migration or oedema, and thus the time between implantation and image acquisition for planning and treatment. Users should also recognize that the application of implanted fiducials is limited to the target, and positional evaluation of organs at risk is not provided.

4.2.2. Image guidance

The type of image guidance to be used for the patient will relate directly to the immobilization and positioning of the patient. Where motion of the target is expected due to respiration, experts recommend the use of time resolved 4-D image acquisition. Potential artefacts due to fiducial markers need to be considered.



FIG. 4. A typical radiotherapy process including IGRT, with the staff involved in each step.



FIG. 5. A typical IGRT process, with the staff involved in each step.

4.2.2.1. Target delineation

The target delineation follows the same principles as 3-D CRT. As consideration of motion becomes explicit in IGRT, the concept of internal target volume (ITV), as defined in Ref. [3], is often useful in this context. For IMRT, the conventions described in Ref. [4] offer appropriate guidance. If fiducial markers are used, a clear correlation between the markers and target volumes needs to be established.

4.2.2.2. Reference images and image guidance protocol

Reference images (e.g. digitally reconstructed radiographs and CT datasets) are required as a basis for images acquired at the time of treatment. The reference images are created in the 3-D treatment planning system and need to be registered to the treatment coordinate system. The transfer of contours for image registration between the reference and verification images is recommended. Contours may include fiducial markers and isodose volumes.

The radiation oncologist, in consultation with the radiotherapy multidisciplinary team, chooses and prescribes the appropriate image guidance protocol.

4.2.3. Verification

If the imaging directive according to the institutional protocol is scheduled in the RVS, the correct scheduling has to be verified. The integration of the IGRT scheduling in the IGRT workstation and the treatment RVS should be verified.

It is important to assess the acquired image immediately for image quality and to determine whether it is fit for its intended purpose. At this point, the images should be checked for any immediately obvious and substantial deviation from planned treatment, and appropriate action should be taken.

The verification image is registered to the reference image to allow quantitative analysis of the accuracy of the initial patient set-up. There are a variety of methods to accomplish image registration. The final responsibility for implementing any change to the patient set-up rests with the RTT, and in some instances, may need input from the radiation oncologist. The output of this step is a record of how the patient set-up was modified (e.g. couch translation or rotation). Appropriate action is taken as per the specified IGRT protocol.

For on-line IGRT protocols, image registration and quantitative analysis take place prior to patient treatment. It is important to verify every patient shift prior to treatment delivery. As on-line decisions have to be made in a timely fashion, clear protocols and workflow and good labelling are required. Integration of the on-line set-up procedures into the linear accelerator control console and RVS software reduces the risk of errors.

4.2.4. Treatment delivery and post-treatment imaging

For advanced IGRT, intrafraction motion is monitored and acted upon as appropriate (see Section 6.8). Post-treatment imaging may be required to check that no significant changes in patient position have occurred during treatment. This may influence the delivery of subsequent fractions.

The off-line process (registration and quantitative analysis) allows for complex decision making. Timely review of off-line images is important to ensure optimal treatment for future fractions. In the on-line process, subsequent off-line review and approval of the images acquired according to the on-line protocol is a good practice to establish the types and sizes of effect, plus any trends, and to deduce possible causes.

5. IMAGE GUIDED RADIOTHERAPY STAFF

5.1. ROLES AND RESPONSIBILITIES

5.1.1. Radiation therapists

The RTT's role in IGRT commences at clinical implementation, where the RTT, along with the radiation oncologist and medical physicist, constitute the IGRT committee. Here, consideration is given to treatment site selection for the initiation of IGRT, as well as market research on equipment selection.

One or more RTTs, together with the radiotherapy multidisciplinary team, will be responsible for the development of education and training materials for RTTs in the initiation of IGRT. These materials should be revised appropriately by the RTT as IGRT is expanded to other treatment sites. These RTTs might also be responsible for the education and training requirements of all RTTs in the department.

One of the fundamental elements of IGRT implementation is the development of IGRT protocols, which clearly define the off-line or on-line workflow procedure, including the documentation that is to be followed for IGRT of each treatment site. The RTT, together with the radiation oncologist and medical physicist, need to contribute to such protocols to optimize the accuracy of treatment delivery. Designated RTTs will also be responsible for quality assurance of the image registrations performed by all departmental RTTs.

5.1.1.1. Imaging and treatment delivery

Treatment delivery with IGRT results in increased roles and responsibilities for the RTT. However, the fundamental aspects of the RTT's role in the accurate delivery of 3-D CRT and IMRT remain unchanged and include: patient positioning and immobilization; accurate acquisition of pre-treatment imaging; treatment planning where appropriate; and all aspects of treatment delivery and care. Level 3 IGRT may require a high degree of patient cooperation, so the RTT should also explain the IGRT process to the patient.

The RTT has greater responsibility and more decisions in both the selection and implementation of the optimal IGRT protocol. This constitutes image acquisition in the treatment room, image registration, evaluation of the acquired images in relation to the reference image dataset and taking action on the resultant quantified shifts or anatomical discrepancies, as appropriate. The RTT also has a responsibility to notify the radiation oncologist as appropriate when action levels are exceeded or cases present that are beyond the scope of the IGRT protocol.

5.1.2. Medical physicists

The role of the medical physicist depends on local practice and the availability of other staff, such as imaging physicists, service engineers and RTTs. Figures 4 and 5, in Section 4, provide an overview of the steps in which medical physicists are involved during IGRT treatments. In addition, they are key to specifying and commissioning the equipment, developing appropriate imaging protocols, and developing and conducting an appropriate quality control programme. Medical physicists are involved in the following:

- Determining the specifications of image guidance tools based on clinical need;
- Performing market research with regard to available IGRT options and their compatibility with existing equipment, procedures and clinical need;
- Advising on immobilization devices and their impact on imaging;
- Advising on the adequacy of fiducial markers for imaging procedures;
- Assessing automatic matching and registration procedures for reference and verification imaging;
- Reviewing the appropriateness and adequacy of reference images;
- Transferring, handling, storing and archiving images;
- Developing protocols for motion management, as appropriate and required.

Medical physicists are responsible for:

- Acceptance testing of IGRT equipment, including dose assessment;
- Commissioning IGRT equipment, including radiation protection of patients and staff;
- Developing imaging protocols that are optimized for the clinical purpose, while minimizing the radiation dose to the patient;
- Developing and conducting quality assurance and quality control procedures for image quality, radiation dose and geometric accuracy;
- End to end testing of the IGRT process;
- Performing calculations of patient shifts in off-line IGRT protocols;
- Collating and analysing institutional data, including action levels;
- Advising radiation oncologists on CTV to PTV margins based on IGRT results.

5.1.3. Radiation oncologists

The role of the radiation oncologist depends on local practice, delegated responsibilities, local rules and regulations, and the types of IGRT protocol to be implemented. Figures 4 and 5, in Section 4, provide an overview of the steps in which radiation oncologists are involved in IGRT treatments. In addition, the oncologists, being wholly responsible for patient outcome, should have knowledge of all the steps in IGRT, including its practical implementation at the treatment unit and quality control. Radiation oncologists are key in assessing, recording and evaluating patient outcomes following the implementation of IGRT. Radiation oncologists are involved in the following:

- Identifying current and future clinical needs for image guidance;
- Performing market research with regard to available IGRT options and their compatibility with the clinical needs, local health care environment and workflow;
- Identifying and prioritizing clinical needs to be met through immobilization devices;
- Evaluating the risks, local feasibility and benefits of fiducial marker implantation, while possibly being directly responsible for marker implantation;
- Approving reference images for the relevant IGRT protocols, including relevant structures and isodose lines;
- Developing protocols for motion management, as appropriate and required;
- Developing imaging and matching protocols that are optimized for the clinical purpose, with an awareness of the impact of additional patient dose;
- Reviewing aggregated IGRT data from the patient population to help to improve the IGRT programme.

Radiation oncologists are responsible for:

- Clinical assessment of patients and prescription of an appropriate course of radiotherapy where indicated, while also communicating the nature of the treatment, its goals and risks to the patient;
- Identifying individual patients who are appropriate for IGRT and prescribing the IGRT imaging protocol;
- Contouring and approving organ at risk volumes;
- Defining gross tumour volumes (GTVs) and GTV to CTV expansions;
- Defining CTV to PTV margins based on IGRT results and clinical trade-offs in consultation with medical physicists and RTTs;
- Performing direct or indirect supervision of patient positioning corrections, including systematic or periodic review and approving on-line and off-line images;
- Making informed clinical decisions in cases of IGRT identified anatomical changes, including plan adaptation strategies.

5.2. STAFF TRAINING

5.2.1. Radiation therapists

Additional education, training and experience in the requirements for IGRT are mandatory for the RTT, and a specified set of learning outcomes should be achieved prior to clinical initiation of IGRT. On completion of the education and training programme, the RTT should be able to:

- (a) Comprehend and perform optimal in-room image acquisition;
- (b) Demonstrate an awareness of the dose associated with various imaging methods;
- (c) Discuss image registration methods, including registration algorithm functionality;
- (d) Perform optimal registration, being cognizant of inter- and intra-observer variation at registration;
- (e) Demonstrate detailed knowledge of radiographic and cross-sectional anatomy as it relates to radiotherapy treatment planning;
- (f) Comprehend the concepts of systematic, random and residual effects and how these relate to IGRT protocols;
- (g) Describe current motion management strategies;

- (h) Critically evaluate acquired images and apply corrections to treatments as per the departmental IGRT protocol;
- (i) Discuss how the quantification of systematic and random effects can determine margin calculation;
- (j) Demonstrate detailed knowledge of the potential dosimetric impact of the application of couch shifts;
- (k) Comprehend and carry out daily quality assurance procedures for the IGRT equipment.

5.2.2. Medical physicists

Many medical physicists have been trained in one specialty. Medical physicists specializing in radiotherapy are only trained in the aspects of diagnostic imaging that pertain to the radiotherapy process. This does not necessarily include image quality optimization and the determination of imaging dose and its interpretation. Hence, either access to a medical physicist specializing in diagnostic radiology is required (e.g. from a radiology department) or the medical physicist specializing in radiotherapy needs to receive adequate training and education in medical imaging physics. In addition to the knowledge, skills and competencies required for 3-D CRT (see Ref. [5]), the following knowledge and skills are required:

- (a) Necessary knowledge:
 - A good understanding of X ray imaging procedures, with particular emphasis on CT;
 - A basic understanding of other imaging modalities, including but not limited to ultrasound and magnetic resonance imaging;
 - A basic understanding of image quality parameters (e.g. modulation transfer function, signal to noise and spatial resolution) and the tools to assess them;
 - Familiarity with common artefacts in CT and CBCT (e.g. motion, metal artefacts and ring artefacts);
 - An understanding of radiation dose delivered in diagnostic procedures, the quantities used to determine it (e.g. CT dose index and dose–length product) and the tools required to assess the dose;
 - Cross-sectional anatomy of common radiotherapy treatment sites;
 - A basic understanding of organ motion as relevant to radiotherapy treatment;
 - An understanding of Refs [3, 4], including the ITV concept;
 - An understanding of random and systematic effects in radiotherapy treatment and their impact on CTV to PTV margins;
 - An understanding of quality control of image quality, including geometric accuracy and imaging dose;
 - An understanding of commissioning and acceptance of diagnostic imaging equipment, including CT and CBCT;
 - A basic understanding of image formats, including DICOM;
 - A sound understanding of image handling, including contrast enhancement and image matching.
- (b) Practical training in the following:
 - Operation of the imaging equipment planned for IGRT;
 - Handling images;
 - Quality control for the imaging equipment planned for IGRT;
 - Assessing and interpreting the radiation dose delivered in diagnostic procedures, including methods for dose optimization.

5.2.3. Radiation oncologists

In addition to the knowledge, skills and competencies required for 3-D CRT (see Ref. [5]), the following knowledge and skills are required of the radiation oncologist engaged in IGRT:

- (a) Necessary knowledge:
 - A basic understanding of X ray imaging procedures;
 - A basic understanding of other imaging modalities, including but not limited to ultrasound and magnetic resonance imaging;
 - A basic understanding of image quality parameters (e.g. signal to noise and spatial resolution);
 - A basic understanding of quality control of image quality, including geometric accuracy and imaging dose;

- A basic understanding of image handling, including contrast enhancement and image matching;
- A familiarity with common artefacts in CT and CBCT (e.g. motion, metal artefacts and ring artefacts);
- An understanding of the radiation dose delivered in diagnostic procedures, the quantities used to determine
 it (e.g. CT dose index and dose–length product), the spatial distribution of the dose in the patient and the
 clinical relevance of the delivered dose;
- A good understanding of general cross-sectional CT anatomy;
- A basic understanding of organ motion as relevant to radiotherapy treatment;
- An understanding of Refs [3, 4], including the ITV concept;
- An understanding of random and systematic effects in radiotherapy treatment and their impact on CTV to PTV margins;
- If relevant, a sound understanding of the indications, contra-indications, risks and benefits of fiducial marker placement;
- An understanding of the uncertainties and limitations of IGRT;
- An understanding of the impact of changes in patient anatomy on the dose delivered to targets and organs at risk;
- An understanding of the clinical impact of random or systematic target/organ at risk misalignment;
- An understanding of dose-volume effects on organs at risk.
- (b) Practical training in the following:
 - Image registration and review;
 - Fiducial marker placement.

5.3. STAFFING REQUIREMENTS

Additional human resources are required to provide an IGRT service owing to the additional complexity in the imaging and treatment. The IAEA has developed a tool to estimate staffing levels in radiotherapy practice [57]. If 400 patients per year are to be treated with Level 2 IGRT, the number of radiation oncologists needs to increase by 0.1 full-time equivalent (FTE) compared to a Level 1 service managing the same number of patients. Similarly, the number of medical physicists needs to increase by 0.2 FTE and the number of RTTs needs to increase by 1.1 FTE. The largest increase is for the RTTs who perform the additional imaging procedures and shifts in set-up, and record the information for subsequent review and analysis.

6. IMAGE GUIDED RADIOTHERAPY IN CLINICAL PRACTICE

6.1. MILESTONES FOR IMAGE GUIDED RADIOTHERAPY

An IGRT programme should be built on a firm foundation of expertise in 3-D CRT. It should not be embarked until certain basic milestones have been reached. Departments that have not reached these milestones are encouraged to engage with Level 1 IGRT concepts, in particular off-line review. The questionnaire given in Appendix I provides a checklist of the steps in the process. Milestones that need to be reached before resources are committed to the establishment of IGRT include the following:

- Facilities are in place for the provision of 3-D CRT (as given in Ref. [5]);
- A demonstration by audit that there is compliance with the Level 1 methodology and tools given in Fig. 1, in Section 4;
- The commitment of the multidisciplinary radiotherapy team to implementing IGRT.

Milestones in the process once the project has started include the following:

- The appointment of sufficient staff to ensure that the existing programme of conventional and 3-D CRT will
 not be compromised;
- A commitment of sufficient resources to maintain the existing radiotherapy service;
- Education and practical training of staff (RTT, radiation oncologist and medical physicist);
- A needs analysis in the context of patient population;
- The purchase of necessary equipment;
- Applications training for the RTT, radiation oncologist and medical physicist;
- The commissioning of IGRT hardware and software;
- The extension of the quality assurance programme to cover IGRT;
- The establishment of IGRT protocols including class based imaging directives.

Milestones after the implementation of IGRT include the following:

- A planned review of IGRT services;
- The extension of services to other treatment sites, taking the previous milestones into consideration;
- A comprehensive external audit of the IGRT service, if available.

6.2. CLINICAL IMPLEMENTATION OF IMAGE GUIDED RADIOTHERAPY

The implementation of IGRT is a stepwise process (see Fig. 6). After the IGRT implementation committee has been appointed, it will assess the clinical needs and determine the priorities for the implementation of IGRT. Specifications need to be developed for the equipment required. In general, there are two scenarios: (i) the purchase of a whole new treatment unit with IGRT; or (ii) the upgrading of an existing treatment unit to have IGRT capability. This publication only pertains to the IGRT components in both scenarios, and it is assumed that the treatment unit fulfils the minimum requirements specified in Section 4 of being equipped with a multileaf collimator and an EPID and connected to an RVS that allows image transfer, storage and remote evaluation of patient shifts.

It is important to allow sufficient time for physics staff training before the equipment arrives, so that trained staff are in place to carry out acceptance testing and commissioning. A complete understanding of all these steps is necessary before successfully beginning a new IGRT programme. The possibility of members of the implementation team visiting a department that is experienced in IGRT to observe the procedures and workflow



FIG. 6. Implementation of image guided radiotherapy.

should be considered. The resources required to establish an IGRT programme are outlined in Section 4 (see Table 3 for the cost of the equipment required).

6.2.1. Acceptance testing

Acceptance testing is the process of verifying that the purchased and installed equipment fulfils the specifications agreed upon in the contract. Acceptance testing is often performed using test equipment and tools provided by the manufacturer. It may also include reference images provided by the manufacturer. If the specifications developed by the IGRT implementation committee are not part of the purchase contract, the acceptance test will follow the manufacturer's documentation. It is advisable for staff to familiarize themselves with these documents prior to acceptance testing which demonstrates that:

- (a) The IGRT equipment is functional. This includes the acquisition of images, adjustment of imaging parameters, and matching of reference and verification images.
- (b) The equipment complies with the relevant standards and regulations. This includes electrical, mechanical and radiation safety.
- (c) The equipment meets the specifications agreed upon in the purchase document. This should include basic image quality and dose to the patient.

6.2.2. Commissioning

Commissioning is the process of testing the system for the intended clinical application within the department. The commissioning activities not only depend on the actual IGRT equipment used, but also on the intended use and all other equipment (hardware and software) the IGRT tools are interfaced with. A detailed discussion of the commissioning programme is beyond the scope of this publication, but the programme needs to be developed and agreed upon before the equipment arrives. Commissioning also typically takes significantly more time than the acceptance testing and can involve all members of the team. Aspects that should be considered when commissioning IGRT include the following:

- (a) Fiducial marker type, if applicable.
- (b) Indications and contra-indications for implantation.
- (c) Time required after implantation.
- (d) Marker migration risk and oedema.
- (e) Visualization for planning.
- (f) Visualization with IGRT.
- (g) Imaging equipment and the protocols used for treatment planning.
- (h) Patient immobilization and set-up for the relevant clinical scenario.
- (i) Contouring of structures, including the development of ITV and PTV.
- (j) Creation of reference images.
- (k) Image transfer from the treatment planning system to the treatment unit and confirmation of a consistent coordinate system from imaging, treatment planning and treatment delivery.
- (1) Internal motion and deformation over the time of delivery.
- (m) IGRT methods:
 - Mechanical accuracy;
 - Manoeuvrability and deployment (default settings) for the safe and appropriate imaging of different disease sites;
 - Image quality;
 - Geometric fidelity and distortion;
 - Artefacts;
 - Time of image acquisition;
 - Image display option;
 - Radiation dose.
- (n) Registration methods for reference and verification images.

- (o) Determination of the action levels pertaining to the differences between the reference and verification images.
- (p) Adjustment of patient or isocentre position as a result of IGRT.
- (q) Recording of data and storage of images.
- (r) On-line and off-line image review and approval policies.

Consideration of the safety of the patients and staff is an important part of commissioning an IGRT system. Interlocks should be tested and procedures should be developed that will prevent unintended patient exposure. All unintended exposures or near misses should be reported according to the radiotherapy department's incident reporting and learning system. Interlocks that prevent collisions of the IGRT equipment with the patient need to be tested during commissioning. Licensing of the X ray generator and X ray tube will also need to be implemented as required by radiation safety and protection legislation and regulations in each jurisdiction [18].

At the end of the commissioning process, at a minimum, the following should be available:

- The report from an end to end test;
- Documentation of all aspects of system performance;
- A description of the scope of service;
- Procedural documents for all staff members relevant to the clinical scenarios;
- Baseline data for quality control activities;
- A schedule of review of practice.

Although the vendor usually provides applications training for the IGRT equipment and associated software at the time of commissioning, either on-site or off-site, this training will not cover all the clinical expertise required for the implementation of IGRT (see Section 5 on staff education and training requirements).

6.3. QUALITY ASSURANCE OF IMAGE GUIDED RADIOTHERAPY

6.3.1. Equipment quality assurance

The imaging equipment for IGRT requires the same type of quality assurance as conventional diagnostic radiology equipment, plus additional quality assurance for image guidance (i.e. positioning). The equipment quality assurance deals with image quality, geometrical accuracy and dosimetry. Given the commonality with general radiological imaging, best practice is to seek advice from, and work with, a diagnostic radiology department for these aspects of quality assurance. Such a department will have the expertise and the necessary dosimetry and phantom equipment. There are six main quality assurance issues to consider:

- Safety systems;
- Generators and X ray tubes;
- Image quality;
- Imaging dosimetry;
- Geometry;
- IGRT software.

Individual IGRT manufacturers have their own systems for quality assurance, including phantoms and associated software. This subsection is meant to be indicative for CT based systems. A fuller discussion of the quality assurance requirements for CT based IGRT can be found in an American Association of Physicists in Medicine (AAPM) report [58]. Other discussions of image quality requirements for imaging systems for a range of radiotherapy imaging approaches can be found in Refs [19, 59–64].

Quality assurance for mechanical and electrical safety systems involves regular inspection and testing of interlocks (e.g. collision avoidance interlocks), warning signs and lights, and patient communication systems.

Quality assurance for generators and X ray tubes involves measurement of the peak tube voltage (kilovolt peak, kVp), timer accuracy and half value layer under standardized conditions, in addition to tube leakage.

Imaging system quality assurance involves monitoring the quality of the images produced plus dosimetry. Image quality is measured using a series of metrics that primarily describe the spatial resolution and contrast performance of the system. The modulation transfer function is often used to quantify the system performance [65]. Phantoms such as the Leeds Test Objects are often used to measure system performance for CT based systems [66]. These phantoms combine regions of high spatial resolution with subtle changes of contrast. Bar patterns of varying resolution are often used for modulation transfer function measurements. The mechanical integrity of a CT based system is essential for image quality. This is often measured by reconstructing an image of a small, high density object, such as a ball bearing phantom. In addition, a more anatomical phantom, such as an Alderson RANDO phantom, can be imaged to perform qualitative quality assurance. Imaging quality assurance should be carried out regularly to monitor any changes to system performance compared to that at commissioning, and following any changes to, or major services of, the treatment unit.

Dosimetric quality assurance for kV X ray systems should be carried out using the standard procedures from radiology [67, 68]. Using a CT dose index phantom and ionization chamber is a standard dosimetry method for CT based systems [69]. Other methods such as the dose–length product have less clear applicability for CBCT systems. For kV planar imaging, measuring the air kerma in air with a large volume ionization chamber (e.g. 6 cm³) at a set distance from the source provides an excellent baseline for monitoring the X ray tube output. The air kerma measurement can be converted to organ dose (e.g. skin dose), with appropriate factors [68].

Quality assurance should be carried out for the geometric accuracy of the imaging system to confirm its correct alignment with the mechanical, optical and radiation isocentres of the linear accelerator. Radio-opaque markers aligned to the mechanical or optical isocentre can be imaged to quantify the extent of alignment.

Quality assurance for the system's application for IGRT involves establishing that the images produced by it are correctly registered to the treatment machine coordinate system for accurate position measurement compared to the planned patient position. The use of a geometric phantom can achieve this quality assurance. In some circumstances, the CT based IGRT images may inform the need for replanning. In this case, more accurate measurement of the CT number may be desirable. This can be achieved using a contrast phantom containing several regions of known electron density. Tables 4–7 present examples of quality control tests for common IGRT equipment taken from a review of Refs [19, 58–63].

6.3.2. End to end tests for image guided radiotherapy processes

Quality assurance not only needs to be performed for IGRT equipment hardware, but also for the processes that underpin IGRT, for example the image transfers from the imaging panel to the linear accelerator console and the RVS. Various end to end tests for IGRT have been proposed [13, 70], while an AAPM report [58] recommends that an IGRT procedure test be performed daily. Such a daily test could involve the following:

- (a) Placing a phantom with internal radio-opaque markers on the treatment couch;
- (b) Applying a known positional shift;
- (c) Imaging the phantom with the IGRT system;
- (d) Using the IGRT software to determine the shifts required from comparison of the daily image to a reference image that has been created by CT simulation of the phantom, transfer of the CT image dataset to the treatment planning system and transfer of the generated reference images to the treatment machine;
- (e) Applying the positional shift (usually with automated couch movement) and reimaging the phantom;
- (f) Checking in the treatment room that the positional shift has been applied correctly.

6.3.3. External review and audit

External or independent review of the department's practices, including IGRT, is considered to be an essential part of a departmental quality management system. The IAEA has developed guidelines for Quality Assurance Team for Radiation Oncology (QUATRO) audits for radiotherapy departments [71], but the 2007 publication does not include IGRT. More recently, the Quality Assurance Audit for Diagnostic Radiology Improvement and Learning (QUAADRIL) process for auditing radiology departments has been developed [72], and aspects of this process could be adapted to IGRT practice involving kV patient imaging. Clinical trials that involve mandatory IGRT for patients in the trial protocol often include a review of IGRT practice as part of trial quality assurance. Examples include various

Frequency	Suggested action level
Daily	Functional
Daily	Functional
Daily	Functional
Monthly	Baseline
Monthly	Baseline
Monthly	Baseline
Monthly	1 mm
Monthly	Baseline
Monthly	Baseline
Monthly	2 mm
Monthly	2 mm
Monthly	Functional
Monthly	Functional
	FrequencyDaily Daily DailyMonthly Monthly Monthly MonthlyMonthly MonthlyMonthly MonthlyMonthly MonthlyMonthly MonthlyMonthly Monthly

TABLE 4. QUALITY CONTROL TESTS FOR ELECTRONIC PORTAL IMAGING DEVICE SYSTEMS

TABLE 5. QUALITY CONTROL TESTS FOR MV CONE-BEAM COMPUTED TOMOGRAPHY SYSTEMS

Test	Frequency	Suggested action level
Safety/mechanical		
Mechanical integrity Electrical integrity Collision interlocks	Daily Daily Daily	Functional Functional Functional
Imaging		
Scale Spatial resolution Contrast Uniformity Artefacts Noise Spatial distortion CT number accuracy Monitor brightness, focus and contrast	Monthly Monthly Monthly Monthly Monthly Monthly Monthly Yearly	2 mm Baseline Baseline Baseline Baseline Baseline 25 HU Functional
Dosimetry		
Dose	Monthly	Baseline
Geometry		
Imaging/treatment/optical coordinate coincidence	Daily	2 mm
Software		
On-screen tools Image matching software Export to treatment planning system	Yearly Yearly Monthly	Functional Functional Functional

Test	Frequency	Suggested action level		
Safety/mechanical				
Mechanical integrity	Daily	Functional		
Electrical integrity	Daily	Functional		
Collison interlocks	Daily	Functional		
Generator/X ray tube				
Kilovolt peak	Yearly	$\pm 5 \text{ kV}$		
Half value layer	Yearly	Baseline		
Output linearity	Yearly	10%		
Head leakage	Yearly	0.1%		
Imaging				
Image quality (high contrast, low contrast, spatial resolution)	Monthly	Baseline		
Artefacts	Monthly	No artefacts		
Noise	Monthly	Baseline		
Spatial distortion	Monthly	1 mm		
Monitor brightness, focus and contrast	Yearly	Baseline		
Dosimetry				
Radiation output (air kerma)	Yearly	Baseline		
Geometry				
Isocentre alignment	Monthly	2 mm		
X ray tube and detector panel position	Monthly	2 mm		
Software				
On-screen tools	Yearly	Functional		
Image matching software	Daily	Functional		

TABLE 6. QUALITY CONTROL TESTS FOR KV PLANAR X RAY SYSTEMS

TABLE 7. QUALITY CONTROL TESTS FOR KV X RAY CONE-BEAM COMPUTED TOMOGRAPHY SYSTEMS

Test	Frequency	Suggested action level
Imaging		
Scale and orientation	Monthly	1 mm, 1°
Uniformity and noise	Monthly	Baseline
High contrast resolution	Monthly	Baseline
Low contrast resolution	Monthly	Baseline
CT number accuracy	Monthly	Baseline
Artefacts	Monthly	No artefacts
Dosimetry		
Axial and skin dose	Yearly	Baseline
Geometry		
Alignment with MV and optical isocentre	Monthly	2 mm
Geometry calibration (Elekta)	Yearly	2 mm
Couch movements	Monthly	2 mm
Software		
On-screen tools	Yearly	Functional
Image matching software	Daily	Functional
Date transfer to treatment planning system	Monthly	Functional

Radiation Therapy Oncology Group (RTOG) trials, such as RTOG 0236 and RTOG 0438, the Ontario Clinical Oncology Group PROFIT trial [73] and the Trans Tasman Radiation Oncology Group BOLART trial [74]. The self-assessment questionnaire in Appendix I could also be adapted for use by external auditors of an IGRT practice.

6.4. UNCERTAINTIES IN IMAGE GUIDED RADIOTHERAPY

It is useful to distinguish between error and uncertainty. Errors should be detected and corrected for, while it is impossible to apply a correction for uncertainty, for which the direction is unknown. However, an estimate can be made of the magnitude of uncertainty. Following the approach of the International Organization for Standardization, uncertainty analysis distinguishes between uncertainties of types A and B [75].

Type A uncertainties are a result of random variations, which are assumed to be normally distributed and can be reduced by performing more measurements. In the case of IGRT, this has important implications, as it allows uncertainty to be reduced for individual patients by combining the information obtained in IGRT from different fractions. Similarly, it can reduce uncertainties and determine otherwise undetectable systematic effects by combining information from many fractions of many patients. Data management is therefore an essential component of a successful IGRT programme.

Type B uncertainties are the best estimates of other parameters that can influence the outcome of a measurement. Their estimation requires a thorough understanding of the process and is commonly subjective. This makes education and training essential for all team members.

It is beyond the scope of this publication to provide a detailed description of all the uncertainties in the IGRT process. A recent IAEA publication, Accuracy Requirements and Uncertainties in Radiotherapy [76], is dedicated to this broad topic. It states that for a range of IGRT solutions, the geometric uncertainty is of the order of 1–2 mm (one standard deviation) and that the accuracy achievable with such systems is 2 mm (see table 15 of Ref. [76]). It is advisable that radiotherapy departments implementing IGRT perform an uncertainty analysis for their own situation, keeping in mind that its main objective is not to reduce the dose but the spatial uncertainty of the dose delivery (see Refs [1, 77, 78] for further information on estimating uncertainties). This analysis could be performed as part of end to end testing of the IGRT process. Important aspects of the overall uncertainty that could be considered include the following:

- (a) Imaging for treatment planning;
- (b) Contouring of structures;
- (c) Calculation of dose distribution and creation of reference images;
- (d) Patient immobilization and set-up;
- (e) Internal motion and deformation over the time of delivery;
- (f) Imaging modality;
- (g) Registration of images;
- (h) Determination of differences between reference and verification images;
- (i) Adjustment of patient or isocentre position as a result of IGRT.

6.5. IMPACT OF IMAGE GUIDED RADIOTHERAPY ON PLANNING MARGINS

Informed by each patient's image datasets, as well as more general disease patterns, GTV and/or CTV are defined for each patient. Because of uncertainties in the target position relative to the treatment beams, a concept needs to be used to ensure adequate dosing of the CTV. In recent decades, this concept was the creation of a target larger than the CTV — the PTV. The expansion from the CTV to the PTV is a compromise between the risks of CTV under-dosage and the risk of toxicity from the irradiation of healthy tissue.

The two main sources of uncertainties in the target are the position of the target within the patient and the position of the patient in relation to the treatment beam. These uncertainties are dealt with using two margins probabilistically added: the internal margin and the set-up margin.

The uncertainties created by these margins are both random and systematic in nature. There are several published methods for deriving PTV margins, but the most commonly used method is based on the probability

distributions of the cumulative dose over a population of patients. Van Herk et al. [79] show that the PTV margin m_{PTV} is given by:

$$m_{\rm PTV} = \alpha \Sigma + \beta \sigma - \beta \sigma_{\rm p} \tag{1}$$

where

 Σ is the standard deviation of the preparation mean values;

 σ is the mean of the standard deviation of all the treatment execution variations;

 $\sigma_{\rm p}$ is the standard deviation describing the width of the penumbra;

and α and β are scaling parameters depending on the required patient and CTV coverage. Assuming a certain radiation penumbra, a large number of treatment fractions and the goal of ensuring a minimum dose of 95% to the CTV for 90% of the patients (excluding rotations and deformations), then Eq. (1) can be simplified to:

$$m_{\rm PTV} = 2.5\Sigma + 0.7\sigma \tag{2}$$

Appendix II provides an example of CTV to PTV margins calculated from Eq. (2) and based on daily X ray planar imaging of the patient in the treatment position.

A goal of IGRT is to improve the therapeutic ratio through better target coverage and/or decreased normal tissue irradiation. In a general sense, off-line image guidance strategies act on systematic effects and on-line strategies act on both systematic and random effects. Even the best IGRT strategy cannot eliminate all sources of random and systematic effects. Radiotherapy departments need to be prudent in reducing margins [80, 81], as current practices may overlook less frequently measured sources of uncertainty, such as differences in physician contouring or target deformation. With the introduction of on-line IGRT, a logical method for quantifying and reviewing margins is to image the patient post-fraction and record the shifts from the pre-treatment reference [82].

In an example of margin reduction with IGRT, a study of prostate radiotherapy guided by daily imaging of three implanted fiducial markers (with pre-treatment correction of misalignments ≥ 2 mm) concluded that intrafraction motion was the largest residual source of uncertainty and CTV to PTV margins could be reduced from approximately 7 mm to approximately 4 mm [83]. Such margin reductions have been shown in other series to predict reduced rectal toxicity in prostate radiotherapy [84–86].

6.6. JUSTIFICATION AND OPTIMIZATION IN IMAGE GUIDED RADIOTHERAPY

Most IGRT imaging methods deliver an ionizing radiation dose to the patient in addition to the therapeutic dose. Since it is a different irradiated volume, it is important to be aware of what dose is delivered for a single IGRT fraction and for imaging throughout the patient's treatment course and how this compares with the therapeutic dose.

Imaging dose values and their spatial distribution depend on the modality and particular implementation [17]. Doses for kV-CBCT can be of the order of 1 cGy [87], with MVCT doses of several cGy [88]. Doses for kV planar imaging vary depending on imaging strategy, with values in the range of 0.1 mGy and 2 cGy [28]. In comparison, MV portal imaging typically requires treatment beam doses of the order of 10 cGy to acquire an image [89]. The prescribed therapeutic dose to the isocentre can be 40–70 Gy, depending on the treatment site and fractionation regime. Diagnostic CT doses are often quantified using a CT dose index [90] and dose–length product [91]. Therapeutic doses are measured in terms of the dose to the target and the distribution around that dose. It is important to note that for kV dosimetry, the dose to bone can be two to three times higher than the dose to soft tissue [92].

It is important that all medical radiation exposures be appropriately justified, as stated in Requirement 37 of GSR Part 3 [18]. For the radiation oncologist, this means that the IGRT procedure for each patient needs to be clearly and unambiguously prescribed, along with the therapeutic dose. In prescribing the frequency and type of IGRT procedure, the radiation oncologist needs to be aware of the risks as well as the benefits. The risk is secondary cancer induction from the dose associated with the IGRT procedure, while the benefit lies is in the potential for a reduction in the volume of non-cancerous tissue irradiated to high doses and the consequent reduction of acute and

chronic radiation side effects. Experts also advise that a record be maintained of all patient imaging procedures and that the oncology information system is specified to perform this function. It is the responsibility of the medical physicist to advise the radiation oncologist of the expected dose from each type of IGRT procedure. It is also the responsibility of the medical physicist to ensure that the IGRT procedure is optimized in terms of minimization of dose, for example by determining appropriate kV, tube loading and collimation settings for each IGRT procedure. Default factory settings of kV and tube loading from the manufacturer should be used as a starting point when determining appropriate settings. The importance of seeking the advice of diagnostic radiology medical physicists for optimization for radiology. There are a variety of directives and guidelines that comment on therapy and imaging doses (e.g. Council Directive 2013/59/Euratom [93]). The radiation oncologist and medical physicist should be aware of these.

In summary, it is important that IGRT imaging doses are justified, prescribed and reported. The context should be considered in the justification — the patient characteristics, the disease site and the prognosis.

6.7. CLINICAL OUTCOME MONITORING

The aim of IGRT is to improve the therapeutic ratio of radiotherapy, often by reducing toxicity while maintaining treatment efficacy. It is important to be able to audit the success of this aim as part of the IGRT programme. For example, if reduced PTVs no longer provide a sufficient margin, the likelihood of a recurrence will be increased. Experts therefore strongly recommend that a database be established when the IGRT programme is initiated so the impact of the programme on patient outcomes can be monitored. A regular review of these outcome data should be carried out. An indication of the benefits to be expected from such a review can be found in the report of the Clinical Outcomes Working Group [94].

6.8. SPECIAL CONSIDERATION OF RESPIRATORY MOTION MANAGEMENT

Both targets and critical structures may move during the time it takes to deliver a radiotherapy treatment fraction. This motion can be divided into regular motion, such as breathing, and irregular motion, such as swallowing or the bowel filling. Most motion management strategies target regular motion, with respiratory motion being the most commonly used.

It is beyond the scope of this publication to cover motion management in great detail and guidance and reviews of this topic can be found in Refs [77, 95, 96]. However, IGRT is considered to be an essential component of motion management, and many of the issues explored in Section 4.2 are applicable to motion management. Respiratory motion management should be considered at several points in the radiotherapy process.

6.8.1. Motion management in patient set-up

Patients undergoing radiotherapy need to be set up to optimize radiation delivery (e.g. hands above head) while being comfortable enough to be able to remain still for the duration of the delivery. Comfortable positioning also makes it more likely that patients relax and breathe quietly, which reduces motion. Specialized immobilization devices such as dual vacuum bags or compression devices can reduce tumour excursion due to breathing.

6.8.2. Motion management in treatment planning

The most common method of motion management is to take motion into account when designing margins. The concept of the internal margin developed by the ICRU [3] includes respiratory motion as one contributing factor to the internal margin. If an ITV concept is used, there is no need to modulate the radiation delivery. The disadvantage of using ITV is the potential for a large margin, which results in the inclusion of large volumes of normal tissue in the treatment fields.

One established method for determining the ITV is 4-D CT [97]. In this method, planning CT scans on the CT simulator are correlated with a signal representing the breathing motion of the patient. The respiratory signal is obtained from a transducer related to a marker or belt attached to the patient's chest. In one approach, the extent

of the motion of the tumour is extracted from the maximum intensity projection formed by taking maximum voxel values from all CT datasets throughout the breathing cycle [98]. Another approach is to delineate the GTV in all phases and create an enveloping contour, or to interpolate between the inhale and exhale phases. Clearly, different methods exist, and it is the user's responsibility to recognize the specific usage and limitations of the approach being employed. It should also be noted that the ITV derived from a 4-D CT is based on a reconstruction during a limited number of breathing cycles on the CT scanner, and might not be representative of the motion amplitude on the treatment machine. Some studies have shown that the amplitude observed on CT underestimates that observed during X ray fluoroscopy. However, Guckenberger et al. [99] show good correlations between the amplitudes obtained from different 4-D CT sessions.

6.8.3. Motion verification prior to treatment

If motion has been taken into consideration, it is important to verify prior to treatment that the motion included in the treatment plan is similar to that observed at the time of treatment. IGRT provides a number of tools for this purpose, such as fluoroscopic X ray imaging and the assessment of blurring in CBCT. Gated 4-D imaging may be another method to assess motion. Fiducial markers have the potential to make motion assessment prior to, or even during, treatment easier.

6.8.4. Motion management in treatment delivery

Treatment delivery can take motion into consideration. Several general approaches can be distinguished:

- Gated delivery turns the treatment beam on and off depending on the phase of the breathing cycle.
- Couch movement can be used to reposition the patient daily following 4-D pre-treatment imaging to determine the average position of the target for that particular day.
- The treatment fields can be adjusted or repositioned to track the target motion during treatment.
- Treatment is delivered using a breathing technique, which could be voluntary, controlled or restricted using abdominal compression.

Examples of current motion management strategies are given in Refs [46, 97, 100–109]. Patient selection criteria are important for all strategies [77].

Appendix I

SELF-ASSESSMENT QUESTIONNAIRE

This questionnaire is designed to assist radiotherapy departments planning to embark on a programme of IGRT in checking that they have all the necessary requirements. By the time the first patient is to be imaged with the IGRT system, the answers to all the questions should be "Yes". Where gaps are identified, they will need to be addressed.

- (1) Does your department meet the requirements for 3-D CRT listed in the self-assessment questionnaire in IAEA-TECDOC-1588, excluding IMRT (questions 1–49)?
- (2) Have one or more patient groups been identified that would benefit from IGRT?
- (3) Have all groups of staff had at least one year of experience in the planning and delivery of 3-D CRT?
- (4) Has an IGRT committee including a radiation oncologist, medical physicist and radiation therapist been established to oversee the introduction of IGRT?
- (5) Are there sufficient radiation oncology, medical physics and radiation therapy staff to ensure that the introduction of IGRT does not compromise other radiotherapy treatment, including 2-D and 3-D CRT?
- (6) Are there satisfactory service support arrangements to ensure that the IGRT equipment can be maintained at the required level of accuracy?
- (7) Have all groups of staff had additional education and training in IGRT as appropriate to their discipline?
- (8) Does your department have access to a dose assessment system for IGRT dosimetry?
- (9) Does your department have quality control expertise, methodology and tools to maintain an IGRT service?
- (10) Have image acquisition protocols been developed for the anatomical sites to be treated with IGRT?
- (11) Have IGRT protocols been developed for the anatomical sites to be treated with IGRT?
- (12) Has a database been established to facilitate the recording, analysis and review of patient shift data?
- (13) Have tests been carried out to ensure that the RVS is capable of supporting IGRT (including image review and approval)?
- (14) Have commissioning tests, including end to end tests, been performed to demonstrate IGRT system capability and workflow?
- (15) Have contingency plans been developed in case of unavailability of IGRT?
- (16) Has a mechanism been established to monitor the impact of the IGRT programme on institutional CTV to PTV margin definition, action levels, institutional procedures and clinical outcomes?

Appendix II

EXAMPLE CALCULATION OF A CTV TO PTV MARGIN

In this example, the use of Eq. (2), in Section 6.5, is demonstrated, wherein a CTV to PTV margin is calculated based on displacements recorded between the reference image and in-room orthogonal images in the superior–inferior (S–I), right–left (R–L) and anterior–posterior (A–P) directions. The displacement and margin calculations are shown in Tables 8 and 9. Five patients are treated with the same technique for 25 fractions and orthogonal kV images are taken daily. All measurements are in millimetres. Note that the calculated margin is not inclusive of all uncertainties, and additional margins will be required for other uncertainties, such as volume delineation. These additional margins will need to be added in quadrature to the margin calculated from the recorded shifts [56, 110].

		Patient 1			Patient 2			Patient 3		Patient 4			Patient 5		
Fraction	S–I	R–L	A–P	S–I	R–L	A–P	S–I	R–L	A–P	S–I	R–L	A–P	S–I	R–L	A–P
1	-5	-4	0	2	1	-2	-2	-2	7	4	4	-4	-1	-1	-5
2	2	1	4	-3	-6	-3	-1	1	6	3	-6	-2	4	1	-3
3	-2	-4	1	2	-2	1	4	0	-2	1	2	-2	-3	4	1
4	0	1	4	-1	-5	2	3	0	-2	4	0	-1	2	-2	-4
5	3	1	5	-5	-5	3	-2	4	4	3	2	4	1	4	-5
6	-2	2	0	1	-2	4	3	-4	6	2	2	-2	4	3	1
7	4	1	6	-1	-1	5	-2	-3	-3	1	-5	7	-2	-3	-2
8	-4	-2	2	-4	-7	-4	-1	2	4	1	-5	-3	4	-1	2
9	-5	-3	-3	-4	0	1	-2	-2	5	-5	-5	6	1	3	3
10	-2	-3	5	-1	2	-1	3	0	1	-3	1	1	-4	1	-4
11	-2	1	4	-1	2	4	-1	-2	6	1	-6	-2	-3	1	-4
12	4	1	0	0	-2	-3	-2	-3	1	-3	4	2	1	4	-6
13	0	2	0	2	1	1	3	-4	-1	5	-6	-3	-4	1	3
14	4	1	0	-5	1	-1	2	-2	1	5	-5	6	-3	5	2
15	-2	-1	-2	-5	1	-1	0	-1	3	1	0	4	0	2	-5
16	4	1	2	1	-4	0	4	3	2	-4	0	6	1	3	2
17	1	-4	0	-4	-3	4	2	0	6	4	-3	7	-5	-1	-5
18	5	-1	2	2	-3	0	-2	3	0	-4	-5	7	-4	-3	-3
19	1	2	8	0	-1	-4	-2	1	-1	0	0	-1	4	4	0
20	4	-4	3	-4	-2	-3	-2	-1	2	-1	-6	6	0	0	0
21	3	-2	6	3	1	-2	1	-2	4	2	4	-2	-1	3	0
22	-3	0	-3	-3	-6	3	-2	2	-2	4	-1	5	-3	5	-4
23	3	-1	5	2	-1	0	3	-2	-2	0	1	5	-2	0	-3
24	4	-5	4	0	3	-1	0	3	2	-6	2	-4	4	4	3
25	5	-3	6	-3	2	1	1	-1	-2	0	-5	9	-5	-3	-4
Mean	0.8	-0.9	2.4	-1.1	-1.3	0.1	0.3	-0.4	1.9	0.6	-1.5	2.0	-0.5	1.4	-1.6
SD	3.2	2.4	3.0	2.6	2.8	2.6	2.3	2.3	3.1	3.2	3.6	4.3	3.1	2.5	3.0

TABLE 8. EXAMPLE OF MARGIN CALCULATION FROM RECORDED DISPLACEMENTS

		Fraction	
	S–I	R–L	A–P
SD of the means, Σ	0.8	1.2	1.7
Mean of the SDs, σ	2.9	2.7	3.2
CTV to PTV margin $(2.5\Sigma + 0.7\sigma)$	4.0	4.8	6.5

TABLE 9. FURTHER CALCULATIONS BASED ON THE DATA IN TABLE 8

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ABBREVIATIONS

3-D CRT	three dimensional conformal radiotherapy
AAPM	American Association of Physicists in Medicine
CBCT	cone-beam computed tomography
СТ	computed tomography
CTV	clinical target volume
DICOM	Digital Imaging and Communications in Medicine
e-NAL	extended no action level
EPID	electronic portal imaging device
GTV	gross tumour volume
ICRU	International Commission on Radiation Units and Measurements
IGRT	image guided radiotherapy
IMRT	intensity modulated radiotherapy
ITV	internal target volume
kV	kilovoltage
kVp	kilovolt peak
MV	megavoltage
MVCT	megavoltage computed tomography
NAL	no action level
PTV	planning target volume
RTT	radiation therapist (also known as radiation therapy technologist)
RVS	record and verify system
SAL	shrinking action level

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