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On target 2: updated guidance for image-guided radiotherapy

Radiotherapy Board

June 2021

Contents

Foreword

This report was commissioned by the Radiotherapy Board to support the continued application of image-guided radiotherapy (IGRT) and to enable the future implementation of four-dimensional (4D) adaptive radiotherapy (ART) throughout the United Kingdom (UK). The 2008 report ***On Target: ensuring geometric accuracy in radiotherapy*** (published jointly by the Society and College of Radiographers (SCoR), the Institute of Physics and Engineering in Medicine (IPEM) and The Royal College of Radiologists (RCR)) recommended best, evidence-based practice for geometric treatment verification at a time when kiloVoltage (kV) and three-dimensional (3D) volumetric imaging were emerging, hence the focus was primarily on megavoltage (MV) imaging.[1] A later report, produced in 2012 by the National Radiotherapy Implementation Group and commissioned by the National Cancer Action Team, provided an update to On Target and included volumetric and fiducial marker imaging.[2] Both documents were reviewed to provide the basis for this updated guidance, which includes new and emerging technology and practice.

The principles of effective IGRT applications remain the same. IGRT is a core component of modern radiotherapy services and requires a multiprofessional team approach. It is the responsibility of each therapeutic radiographer, clinical scientist specialising in radiotherapy physics, dosimetrist and clinical oncologist (and all clinical practitioners) to ensure that they maintain and update their skills and knowledge as technology evolves.

The Radiotherapy Board would like to thank Dr Kevin Franks, Dr Helen McNair and Professor Marcel van Herk for their dedication and hard work in leading the development of this new guidance. They were ably supported by a steering group comprising Sophie Alexander, Aileen Duffton, Professor Maria Hawkins, Dr Ann Henry, Professor Andrew Reilly and Dr Sam Tudor, and by a large working group of radiotherapy professionals (see Acknowledgements). We extend our thanks to all of them for their support, their time and their expert contributions.

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References

1. The Royal College of Radiologists, Society and College of Radiographers, Institute of Physics and Engineering in Medicine. *On Target: ensuring geometric accuracy in radiotherapy*. London: The Royal College of Radiologists, 2008.
2. National Cancer Action Team. *Image guided radiotherapy: guidance for implementation and use*. National Radiotherapy Implementation Group report. London: National Cancer Action Team, 2012.

Executive summary

Image guidance (including ART) is an essential component of radiotherapy.

The role of image guidance is primarily to ensure treatment delivery uncertainties are minimised. However, there are remaining uncertainties that should be assessed to ensure the clinical target volume receives the intended dose.

This report describes and recommends the best evidence-based practices for image-guided radiotherapy (IGRT). It also provides guidelines as to how individual centres may implement and/or optimise image-guidance processes locally.

Summary of main recommendations

When establishing an IGRT service development strategy, the entire patient pathway should be considered from the time of radiotherapy consent to radiotherapy planning, and continuing throughout treatment, for every patient receiving IGRT as part of their radiotherapy treatment. The frequency, imaging dose and complexity of the IGRT process should reflect the treatment intent, anatomical site and fractionation (as detailed in the site-specific guidance in Section 10).

Effective immobilisation is critical. Achieving reproducibility during radiotherapy planning and treatment involves reducing both patient bony anatomy motion and internal organ motion. This may complement or even reduce the need for intensive IGRT techniques.

Each radiotherapy centre should have in place site-specific IGRT protocols that are tailored to the needs of that site and take into account the factors affecting the accuracy of set-up. It is the responsibility of each therapeutic radiographer, clinical scientist specialising in radiotherapy physics, dosimetrist and clinical oncologist (and all clinical practitioners) to ensure that they maintain their skills as technology evolves.

Routine prospective IGRT data collection for the individual patient, individual treatment protocol and anatomical sites is essential to calculate systematic and random errors and inform local margins. Data collection and analysis is one of the most critical aspects of IGRT, to ensure and maintain safe implementation and use. Once the accuracy of dose delivered to a target volume is established, IGRT – through research studies or prospective audit – may enable margin reduction and/or facilitate dose escalation to further improve outcomes.

Clinical trial participation is encouraged to develop and implement IGRT protocols safely and efficiently.

Only by including these principles in routine clinical practice can we ensure that patients receive high-quality and effective radiotherapy treatments.

1. Introduction

1.1 Purpose

The purpose of this report is to recommend best, evidence-based practices for image-guided radiotherapy (IGRT, including ART) and to provide guidelines for the local clinical implementation and optimisation of these practices.

The scope of this report includes current and emerging treatment verification methods commonly available in UK departments for all treatment sites, complexities and intents. It does not include paediatric radiotherapy and particle radiotherapy but many of the same principles would apply to those fields.

1.2 Objectives

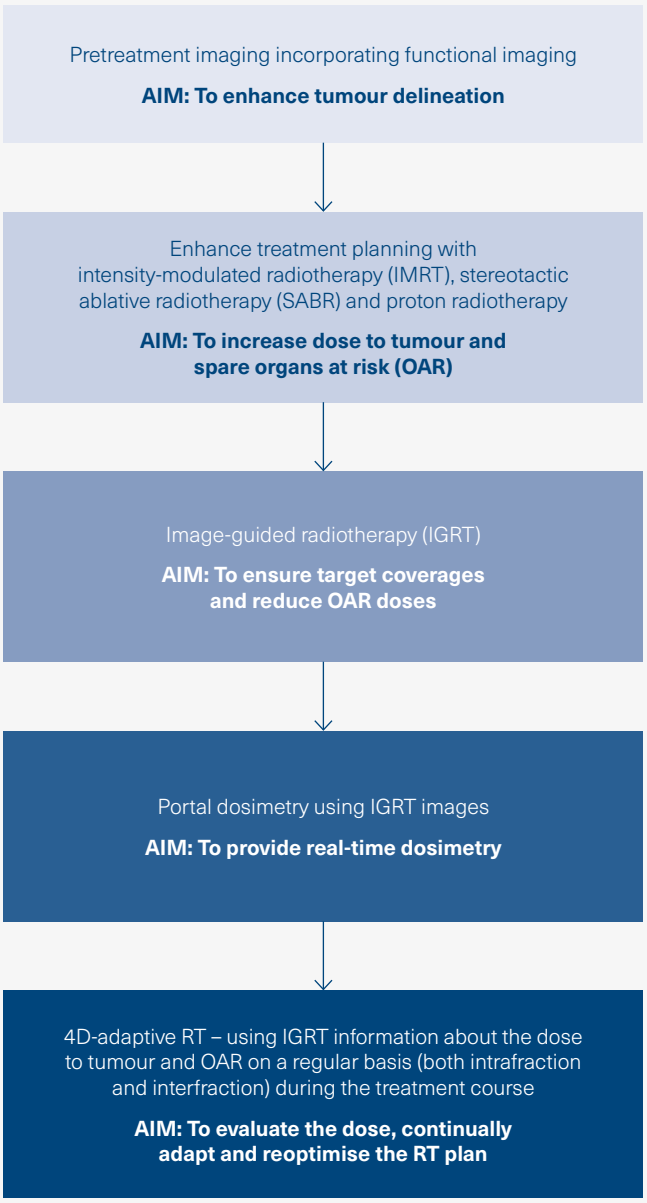
This report has two main aims.

- To provide evidence-based, recommended guidelines for implementing and optimising IGRT in clinical practice.
- To provide guidance for radiotherapy centres to create local management structures, processes and protocols that would aid the implementation of IGRT practices. This includes describing methods by which each centre can determine:
  - The optimal local image-guidance protocols required
  - Site-specific and individual patient systematic and random errors that remain after the image guidance process, which can be used in defining treatment planning margins.

1.3 Background

A report published in 2007 by the National Radiotherapy Advisory Group (NRAG) – *Radiotherapy: developing a world class service for England* – set the national strategy for radiotherapy and has been the template for development of services.[1] The expectation in this report was that four-dimensional ART (4D-ART) would become the standard of care. The NRAG report advised that image-guided 4D-ART was the future standard of care for radical radiotherapy treatment to which the National Health Service (NHS) should aspire . However, the use of 4D-ART remains outside routine clinical practice and is currently under intense investigation. As outlined in the 2012 report *Image guided radiotherapy: guidance for implementation and use*,commissioned by the National Cancer Action Team (NCAT) and produced by the National Radiotherapy Implementation Group, the roadmap to 4D-ART involves many key stages (see Figure 1).[2] For the purposes of this guidance, the NRAG-defined term 4D-ART relates to real-time ART (see Section 7.4).

Figure 1. The roadmap to 4D-adaptive radiotherapy (4D-ART)



On target: ensuring geometric accuracy in radiotherapy, published in 2008 by the Society and College of Radiographers (SCoR), the Institute of Physics and Engineering in Medicine (IPEM) and The Royal College of Radiologists (RCR), defined the core principles and practice of IGRT with recommendations for its implementation into routine practice in the UK.[3] Since the publication of *On target*, IGRT has moved predominantly from two-dimensional (2D) MV image verification to three-dimensional (3D) kiloVoltage (kV) volumetric imaging, and verification through other forms of IGRT (for example, fiducial markers, ultrasound and external surface tracking) is also now routine. The NCAT report, written by the National Radiotherapy Implementation Group – *Image guided radiotherapy (IGRT): guidance for implementation and use* – published in 2012 included the newer forms

of IGRT and newer radiotherapy techniques and indications (for example, stereotactic ablative radiotherapy (SABR)).[2]

The aim of this report is to update the *On target* and NCAT publications using the principles established in both to facilitate the widespread uptake and use of recommended forms of IGRT for each treatment site and indication across the UK.

References

1. Department of Health. *Radiotherapy: developing a world-class service for England*. London: Department of Health, 2007.
2. National Cancer Action Team. *Image guided radiotherapy: guidance for implementation and use*. National Radiotherapy Implementation Group report.London: National Cancer Action Team, 2012.
3. The Royal College of Radiologists, Society and College of Radiographers, Institute of Physics and Engineering in Medicine. *On target: ensuring geometric accuracy in radiotherapy*. London: The Royal College of Radiologists, 2008.

2. What is image-guided radiotherapy?

IGRT is any imaging at the pretreatment and treatment delivery stage leading to an action that can improve or verify the accuracy of radiotherapy delivery.

IGRT encompasses a wide range of techniques from simple visual field alignment checks through to the more complex volumetric imaging that allows direct visualisation of the radiotherapy target volume and surrounding anatomy. Recently several forms of ART have been introduced which, for the purpose of this report, will be considered as part of the framework of IGRT.

2.1 Verification definitions

Many verification terms are used in this report. The following section describes their specific meanings to set the common language used throughout. Other definitions used in this report are given in the Glossary.

2.1.1 Verification

This is the process by which the accuracy of a fraction of radiotherapy is assessed. It is achieved by comparing images (or data) of the treatment delivered with that planned. This will use information from 2D, 3D or 4D systems to give different translational and rotational set-up data.

2.1.2 Reference image

The reference image obtained shows the planned geometry of the treatment field placement relative to internal anatomy or anatomical surrogate such as bone or markers representative of the target. This is used as the standard against which treatment images are assessed. Reference images are produced in numerous ways including: digitally reconstructed radiographs (DRRs), digitally composited radiographs (DCRs), digitised films, ultrasound, scanned patient surface or the entire volumetric planning data set. In this report, 'image' is used to encompass all of these modalities.

2.1.3 Image-guided radiotherapy (IGRT)

In its broadest definition, this applies to all parts of the radiotherapy process from using imaging to define and delineate the target volume to evaluating treatment response.

The most widely used concept of IGRT is using imaging in the treatment room either immediately before or during treatment to evaluate and correct set-up errors.

Images may be acquired using computed tomography (CT) (kV and MV), portal images (MV), kV planar radiographs, ultrasound or other methods.

Despite improved imaging, it is not possible to correct for all components of geometric error in radiotherapy. There are inevitably residual errors (to be accounted for in margin calculations), which may arise from sources such as target delineation uncertainty and movement of the patient or internal motion of organs as the treatment is being delivered (see Section 6).

2.1.4 Offline treatment verification

This compares the reference images with the images taken in the treatment delivery room and analyses the set-up after the treatment has been given. The set-up data are not acted on until the next treatment.

2.1.5 Online treatment verification

This compares the reference images with images taken in the treatment delivery room immediately prior to the treatment being delivered. Any necessary corrections are applied before the treatment is delivered.

Ideally, the time taken between online verification and treatment delivery should be as short as possible (a few minutes) to reduce the variation that may occur from patient movement during this time. Beyond this timescale, the information may no longer represent the patient's true position during the therapy and repeat imaging may be necessary.

2.1.6 Interfractional verification

This evaluates the set-up and motion *between* different treatment fractions.

2.1.7 Intrafractional verification

This evaluates the set-up and motion *during* a single treatment fraction delivery.

The effect of intrafractional movement can be accounted for in treatment margins and, if significant, can be reduced using the following methods:

- Terminating the treatment beam if movement occurs outside predefined tolerances
- Timing the treatment beam to ensure delivery of radiation coincides with a known position of the patient's internal anatomy (gating)
- Restricting variation in the position of internal anatomy.

2.1.8 Real-time treatment verification

In contrast to online imaging, real-time treatment verification is where comparisons are made between the reference images and images taken in the treatment delivery room as the radiation is being delivered.

Most real-time verification methods detect displacements over a predetermined level, so that the operator or automated system can stop, or gate, the treatment.

Other real-time systems use the relationship between external references and internal anatomy. Optical surface detection systems work on a similar principle, by stopping treatment if the patient's external skin contours or reference points move outside a set tolerance level. This method of real-time verification, which often does not use ionising radiation, relies on the assumption that the relationship between external reference points and internal anatomy remains constant.

3. Prerequisites for geometric verification

3.1 Imaging infrastructure

After consideration of the particular anatomical site, each department should decide on a clear method for image guidance, which will depend on the available equipment. These methods may be broadly categorised as:

- 2D planar – MV, kV or magnetic resonance imaging (MRI)
- 3D volumetric – kV cone-beam CT (CBCT), megavoltage CT (MVCT), MRI or ultrasound
- 4D volumetric – kV-CBCT, MRI or ultrasound
- External anatomy surface-based.

In most of the above categories, implanted markers or clips from surgery can be used as surrogates to aid target localisation. Mostly such markers are visualised with planar imaging systems, but transponder-style markers also exist that are tracked electromagnetically and do not require imaging equipment.

Methods such as surface tracking or ultrasound will require the installation of additional equipment within the pretreatment imaging and treatment room. Careful consideration of room layout may then be necessary to accommodate this additional equipment especially if it is to be 'retro-fitted' into an existing treatment space and practical considerations must be taken into account. Room surveys are usually carried out in conjunction with equipment manufacturers to determine the best mounting locations for the supply of power and network cables and to avoid conflict with existing resources such as closed-circuit TV cameras and wall-mounted laser systems.

The method chosen will dictate the requirements for reference image generation done at CT simulation and/or radiotherapy planning, as well as treatment image acquisition on the treating machine. While many systems provide bespoke software for performing image analysis they may or may not be supplied with systems for data management and storage. Where systems are required to interface with existing equipment, issues of networking and connectivity will need to be considered. It will be necessary to establish quality standard operating procedures together with appropriate quality assurance (QA) tests to monitor and maintain the quality of image guidance. Finally, it is important to ensure the consistency of image interpretation across the department. Display quality and viewing conditions should be optimised and ideally should be included in the QA programme.[1]

3.2 Connectivity

The majority of verification equipment requires some form of connectivity to existing equipment even if just for the importation of reference images and/or associated structure sets, such as planning target volumes (PTVs). Manufacturers will commonly employ recognised standards such as DICOM (Digital Imaging and Communications in Medicine). In this case the manufacturer must publish a DICOM conformance statement detailing how interoperability with similarly compliant systems may be achieved.

3.3 Data transfer and storage

Image data sets generated by image-guidance systems can be large (especially 3D and 4D volumetric imaging). This requires departments to consider carefully the issues of data transfer and storage.

Data will generally be transferred between CT scanners, treatment planning systems (TPS), virtual simulation software, image-guidance systems and treatment machines. Under such situations the computer network becomes absolutely essential to the effective operation of treatment and verification workflows. Networks for transferring such data need to be:

- Fast – networks for imaging applications should support data transfer to at least 100 megabits/second and preferably 1 gigabit/second; images should be readily available consistent with the requirements of the particular workflow
- Robust and reliable – information technology measures should be in place to guarantee sufficient up-time
- Secure and able to maintain the integrity of reference and verification data.

The data generated from the verification process (images and analysis data) should be subject to suitable back-up and archiving processes and stored so that historical data are readily available. Ideally, all images should be stored so that they can be accessed easily and rapidly in the future for training, research, retreatments, legal cases and the like. Besides the images, the set-up data derived from the images should also be archived and methods provided to retrieve and analyse them. An important issue to be aware of is the potential for data duplication between systems (for example, the same image data may be stored on the CT scanner, TPS, treatment verification system and image-guidance system). This can be mitigated to some extent by an appropriate picture archiving and communication system (PACS), which can rationalise and thus reduce the overall storage burden. Image analysis data should be archived in an appropriate fashion within the record and verify (R and V) system.

A robust policy on data management may need to be adopted depending on how the system itself is organised. For example, some systems may be configured to automatically delete raw data (for example, CT projections) after a set period of time. Other systems may require manual intervention. It is essential that the system itself is able to collect verification data without reaching storage capacity. Note that some organisations may want to keep raw data for research purposes, thereby enlarging storage requirements.

3.4 Quality assurance and image registration accuracy

Each component of the verification process, from the acquisition of planning data to the subjectivity in decision-making by individuals, may have a certain level of error or uncertainty within it. These should be measured so that the overall accuracy of the verification process is known and quantified. This is an important measure when determining planning margins.[2]

QA programmes should be created to ensure all image quality and verification data collection standards are regularly assessed and maintained. Image quality must be optimised for the intended purpose, for instance patient position verification or use in adaptive planning. This should include consideration of image resolution and scaling, signal-to-noise ratio, artefact reduction and Hounsfield unit accuracy. IPEM report 81 details recommended quality-control procedures to ensure the accuracy of imaging systems.[3]

Verification systems should be assessed in terms of:

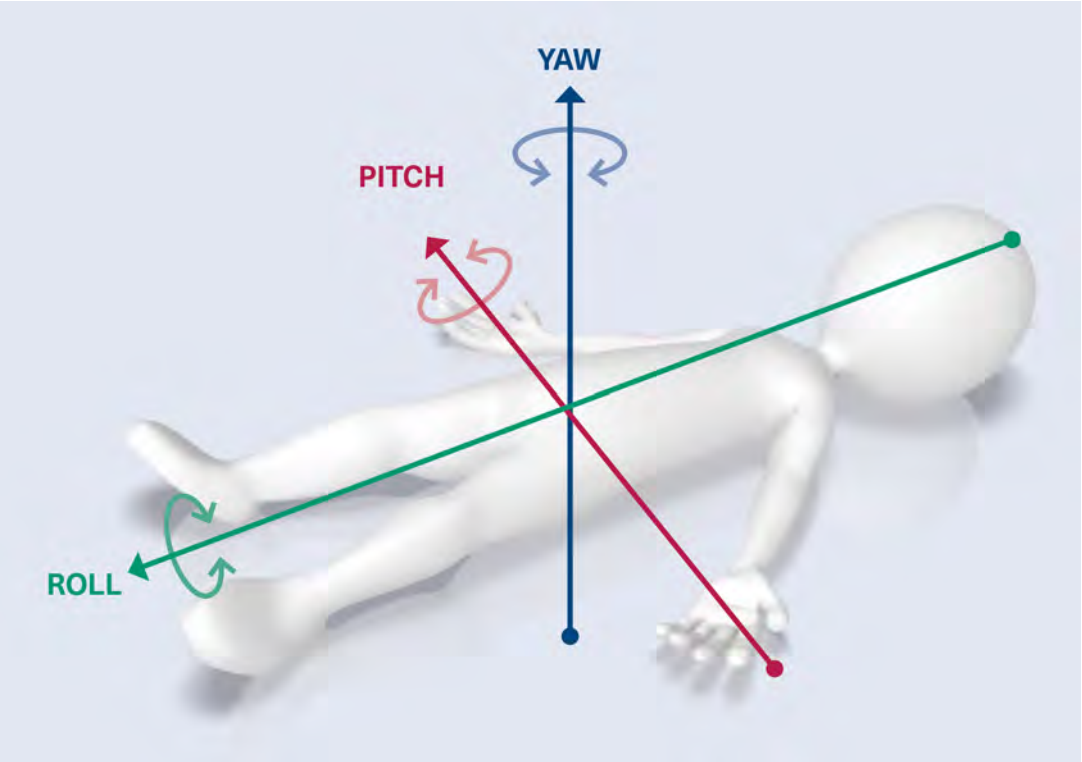
- Image acquisition accuracy and consistency of image quality
- Image processing: how does processing affect the end result (for example, CBCT reconstruction slice thickness, artefact suppression filters)?
- Analysis techniques: how is the accuracy of registration affected by the parameters and methods used (for example, differences between algorithms used, region of interest [ROI] position and size)?
- User accuracy and reproducibility: how do results vary between users, between repeat evaluations and between fractions?
- Accuracy of displayed and performed shifts: how accurate is the displacement information given by each registration system and how accurately is the shift applied?
- Safety: have all steps in the process been reviewed in order to identify all potential errors and have processes been designed to minimise the risk of errors occurring?

3.5 Consistency of co-ordinate systems, error reporting and corrective actions

It is essential within a department to develop clear and consistent conventions and protocols for the reporting and correction of set-up errors. These should be documented in the quality system. Consideration should be given to each of the possible patient orientations on the treatment couch, ensuring that this information is displayed correctly on the images and incorporated into the offset measurements.

- Ideally, a single co-ordinate system should be used across the department, specifying the isocentre position relative to a set-up point, stating translational directions and rotations around these axes. If such consistency between different systems within a department that specify movement is not possible, all co-ordinate systems used in the verification pathway should be clearly documented, along with the conversion process from one to another. The accuracy of the conversion between systems should be tested for every possible patient orientation.
- Protocols should specify the direction of movement and what is moving (for example, the couch or the treatment field).
- In case rotations are analysed in 3D (roll, pitch and yaw), the definitions of the directions of rotations and their order should be properly defined (see Figure 2). The order in which the translations and rotations are corrected may be vendor specific; for example, translations followed by yaw roll and pitch (Hexapod, Elekta) or yaw, pitch and roll followed by translations (TrueBeam [v2.7.2], Varian). This will have an impact on displacements with larger rotations.
- In cases where aspects of the plan are particularly critical, such as due to potential organ at risk overdosage, that information should be communicated to the IGRT team and appropriate guidance given.

Figure 2. Diagram of 3D rotations



Recommendations

- Each department should decide on a clear method for image guidance, which will depend on the available equipment.
- The method chosen will dictate the requirements for reference image generation done at CT simulation and/or radiotherapy planning, as well as treatment image acquisition on the treating machine.
- Image data generated from the verification process should be subject to suitable back-up and archiving processes and stored so that historical data are readily available.
- QA programmes are essential to ensure all image-quality and verification data collection standards are regularly assessed and maintained.
- Each department should have clear and consistent conventions and protocols for the reporting and correction of set-up errors.

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1. American Association of Physicists in Medicine. *Report No. 270 – Display quality assurance*. Report of the American *Association of Physicists in Medicine Task Group 270*. Alexandria, VA: American Association of Physicists in Medicine, 2019.
2. British Institute of Radiology. *Geometric uncertainties in daily online IGRT: refining the CTV-PTV margin for contemporary photon radiotherapy*. London: British Institute of Radiology, 2020.
3. Institute of Physics and Engineering in Medicine. *Physics aspects of quality control in radiotherapy. IPEM report 81*, second edition. York: Institute of Physics and Engineering in Medicine, 2018.

4. Verification equipment and techniques

Good-quality images are essential and treatment image quality should ideally have adequate spatial resolution to visualise the structures of interest with sufficient contrast-to-noise ratio. Acquisition methods should be optimised to produce the quality required.

4.1 Two-dimensional planar imaging equipment and acquisition

4.1.1 Image acquisition and review

Planar imaging with MV and/or kV electronic imaging panels are standard features on most conventional linear accelerators. Two planar images acquired 90 degrees apart allow for measurements in all three directions (superior/inferior, left/right and anterior/posterior) of the target.

2D images can be registered with a 3D planning data set. This allows for identification of 3D rotational set-up variations.

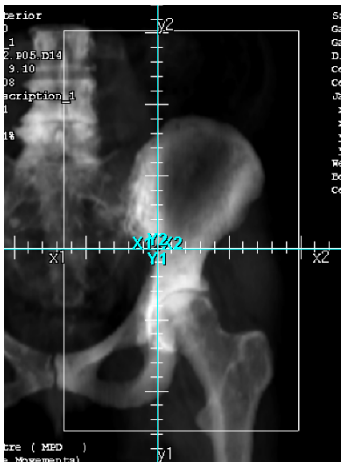
2D kV imaging may also be acquired using a system independent of the linac gantry, such as a detector system mounted on the floor or ceiling.

For linac-based 2D planar imaging, bony landmarks are most commonly used for defining positional variations but surrogates such as fiducial markers may also be used.[1,2,3] Direct lung tumour tracking is also possible.[4,5]

4.1.2 Reference images for 2D image guidance

Traditionally, simulator reference (kV) planar images acquired in the planned treatment position were used as reference images. Such images may be acquired using radiographic film, digital fluoroscopy or digital flat panel. The use of X-ray simulator reference images is no longer recommended because of the introduction of transfer errors. DRRs are reference images generated from the 3D CT data set used for set-up verification (see Figure 3). These may include some processing to enhance structures of interest. Field outlines and isocentre markings may be burnt into the image or provided in the DICOM header. The latter is preferable in case automatic image analysis software is used. DRRs can also be reconstructed as required as part of the 2D to 3D registration process on the treatment machine. This could be useful for imaging non-standard projections and to evaluate large out-of-plane rotations.

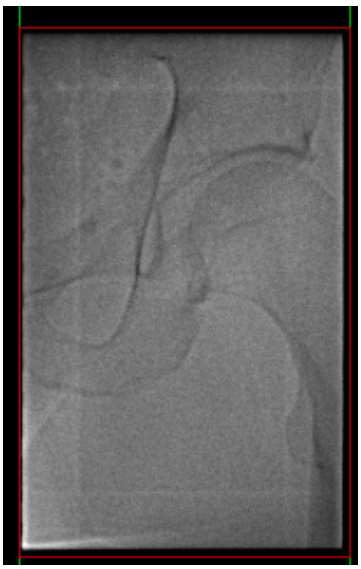
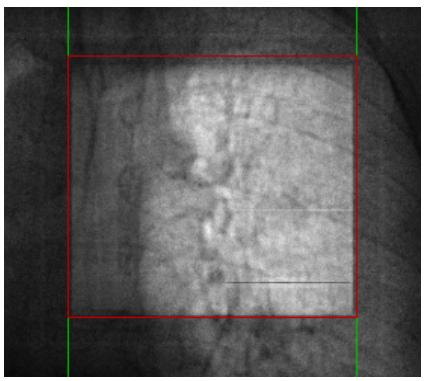
Figure 3. DRR generated from 3D CT data set

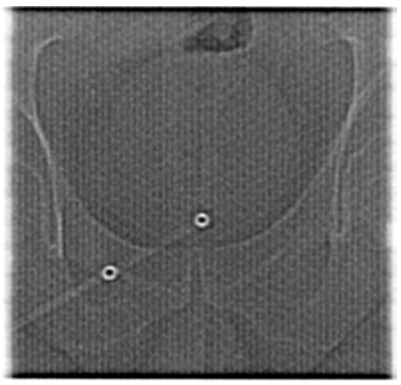
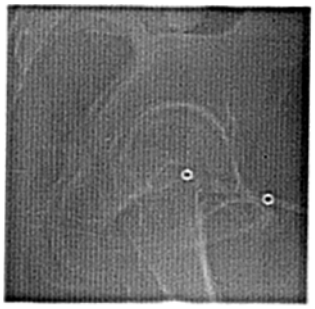
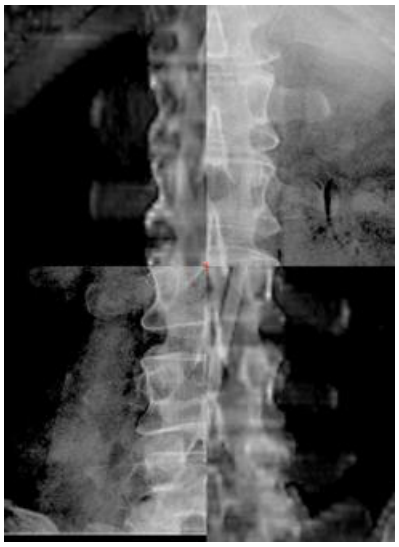


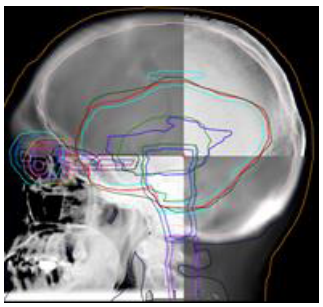
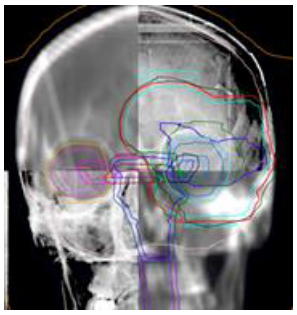
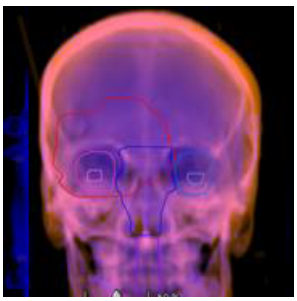
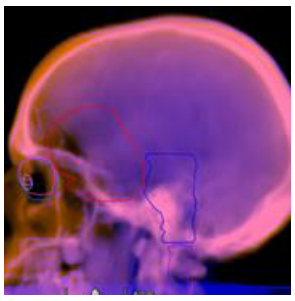
4.1.3 Acquisition modes for 2D image guidance

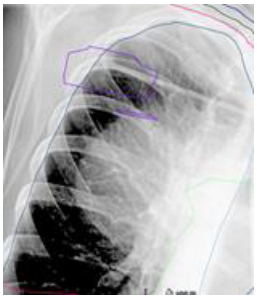
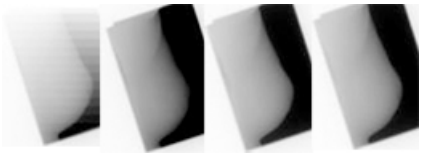
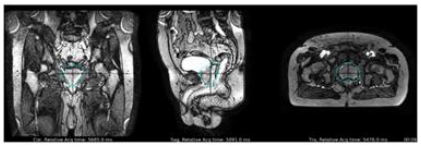
The choice of 2D imaging technique will depend on the treatment site and intent and the local equipment and infrastructure of a department. In general terms, 2D kV imaging provides better contrast between bone and soft tissue and thus bone and soft tissue matching can be clearer than with MV portal imaging. In addition, the dose delivered to the patient is lower, which can be an important consideration particularly when multiple images are required during a treatment course. The following table sets out recommended acquisition modes for different forms of 2D image guidance. Each imaging technique delivers a different dose to the patient. Dose considerations and concomitant exposure are discussed in Section 5.

Table 1. Recommended acquisition modes for different forms of 2D image guidance

Technique	Description	Example
MV single exposure	Single image acquired before treatment. Treatment field defines image size. Suitable if sufficient anatomy is visible. Energies may be chosen different to that of the treatment field. Contrast between bone and soft tissue is not as defined when using higher MV energies compared with images acquired using kV imaging.[6] *(This is due to the dominant interaction being Compton scatter at MV energies).*	*Single MV image.* 
MV double exposure	Used as above, in instances when insufficient anatomy is present in the treatment field to accurately assess set-up errors. Collimator jaws are opened to an appropriate size to see the desired anatomy for a short exposure only. Collimators are then returned to the field size/ shape and a second exposure taken. The two images are digitally added together to produce the double exposure. Delivers extra (concomitant) dose to the patient outside the target volume.	*Double exposure MV image; parallel opposed chest treatment.* 

MV localisation image	Alternative to double exposure, using a single exposure in a field that is specifically created for the image-guided process. This does not correspond to a treatment field.	*MV exposures of large pelvic field.*  
kV single Exposure	Single image acquired before treatment. Image can be added to the treatment field angle or alternatively created at any other useful angle. Image parameters may be adjusted to include only necessary bony landmarks, reducing exposed area and concomitant dose. High contrast between bone and soft tissue. *(This is due to the dominance of the photoelectric effect at kV energies.)* Low contrast between soft tissues. Cannot penetrate metallic implants such as dental work or hip prostheses.[6]	*Checkerboard fusion of kV single – spine treatment.* 

kV/kV paired	Two kV images acquired (as above) at 90 degrees separation. The pair of 2D images is typically registered with the 3D reference data set. Errors in all three directions can be corrected for. When the images are registered to a 3D data set, also rotations can be analysed in 3D. Can be acquired using a linac-mounted kV imager or in-room kV imaging.	*Checkerboard fusion of kV/kV pair – brain treatment.*   *Colour wash fusion of kV/kV pair – brain treatment.*  

MV/kV paired image	As for kV/kV paired imaging but with one MV image and one kV image. Gantry position remains static throughout acquisition. Reduces overall time and risk of patient collision. Higher dose required to that of kV/kV pair but less than paired MV images.	*Medial MV image and kV orthogonal image – breast treatment.*  
Cine loop image	Multiple images (MV, kV or MRI) are acquired throughout all or part of the treatment delivery. Ideal for showing anatomical movement for clinical sites where it may significantly affect the coincidence of the target and the irradiated volume, in particular for hypofractionated treatments. MV imaging can also show motion of the beam collimation system.	*MV cine loop to monitor lung volume.*  *MR images taken to verify target coverage during delivery on an MR-linac.* 

4.2 Three-dimensional volumetric imaging equipment and acquisition

4.2.1 Image acquisition and review for 3D image guidance

Although with 2D planar MV or kV verification it is possible to determine set-up errors by the registration of bony landmarks or implanted fiducial markers, the contrast achieved with 2D planar MV or kV verification is limited. It may not be sufficient for many clinical situations, especially sites requiring good soft-tissue discrimination. 3D volumetric techniques typically produce much better contrast than their 2D analogues; in addition, they produce a full 3D volumetric image for registration to a 3D reference data set, facilitating analysis and visual verification.

Volumetric imaging is when a 3D image is acquired of the patient in the treatment position on the linear accelerator prior to or during radiotherapy being delivered. It allows the internal structures to be visualised including the target and surrounding normal tissue. It enables the target position to be corrected for prior to treatment, along with the ability to monitor changes in the shape of the patient and target or critical neighbouring structures throughout the course of treatment.

4.2.2 Reference images for 3D verification

A reference image for 3D verification is typically a planning CT data set imported from the TPS with structures defined during the planning process such as gross tumour volume (GTV), clinical target volume (CTV), PTV or critical neighbouring organs (organs at risk [OAR]) to aid image analysis. Additional structures such as isodose lines (for example, for 95 per cent PTV coverage and/or OAR dose tolerance limits) can be used. When contrast is used, its effect on image registration for image guidance should be evaluated. For non-CT-based IGRT systems, a compatible reference image may be acquired or generated (for example, in ultrasound or MRI guidance workflows).

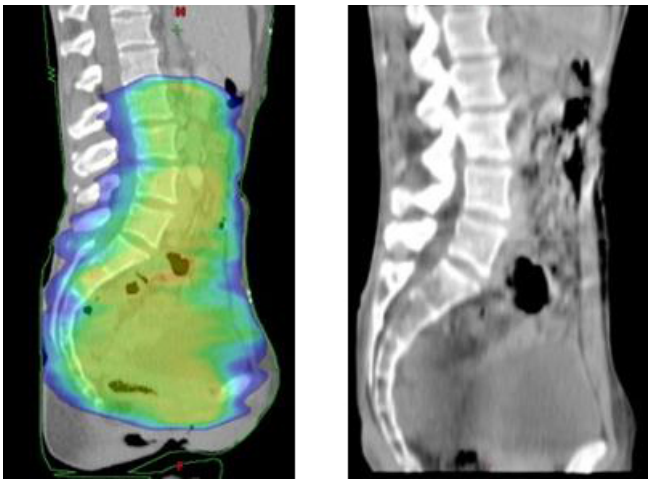
4.2.3 Acquisition modes for 3D image guidance

It is important to establish and optimise several acquisition presets, such as the volume to be acquired and resolution, as this determines dose (as low as reasonably practicable [ALARP]), contrast-to-noise ratio and/or speed (MRI) for different patient groups. Scan length can also be reduced to expose only anatomy that is required for accurate registration. Potential inclusion of a larger volume of healthy tissue receiving dose from volumetric imaging reinforces the need to keep dose ALARP.[7,8] Speed is important as it affects throughput and organ motion increases with time. Tumour motion may be an additional factor in the choice of acquisition preset.

Most manufacturers supply several exposure presets that can help produce a good-quality image. However, these should be adapted to suit individual departmental requirements. It is suggested to link exposure presets to clinical protocols for ease of management.

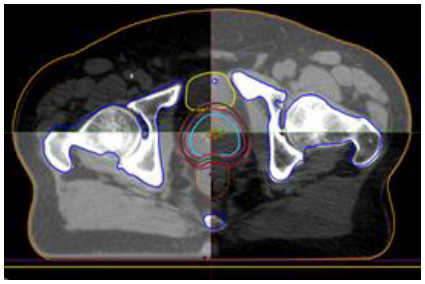
Maximum scan length can prove to be a limitation if the target volume exceeds the scan length restraints. A multi-scan technique can be adopted to overcome this problem on some platforms. Multi-scan is the acquisition of two or more CBCTs, with a predetermined couch long shift carried out in between the scans to ensure minimal overlap. These are fused together to allow image review of an extended volume.

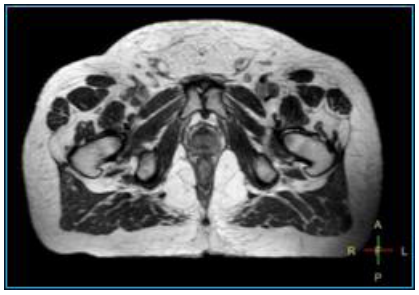
Figure 4. Example of a fused multi-scan CBCT on the right for verification of para-aortic nodal coverage



For CBCT, images can be acquired through a partial arc, which can be stopped and started at different angles or a 360-degree gantry rotation (full arc). The choice of full or partial arc depends on patient size and tumour location. To reduce imaging dose to OAR, stop–start angles can be adjusted. For example, when imaging the head, a partial arc with the source at the posterior aspect of the head would eliminate entry dose through the orbits. Note that different manufacturers have different stop–start angle abilities when acquiring a cone beam.[9,10]

Table 2. Recommended acquisition modes for different forms of 3D image guidance

Technique	Description	Example
kV-CBCT	Cone-shaped kV beam employed and detected on associated flat-panel imager as the gantry rotates around the patient in the treatment position as the linac couch remains stationary.[11,12,13] 3D volumetric data are obtained from the reconstruction of its 2D projections. Some systems have the ability to do iterative reconstruction.[14]	*Checkerboard fusion of CBCT and reference data – prostate treatment.* 

	CBCT data are registered with the planning CT data set. The registration structure (bone, soft tissue or fiducials) will vary depending on anatomical location and requirements of the set-up. Target and OAR structures can be visualised and set-up variations can be measured and corrected prior to treatment delivery.	
MRI	MRI integrated with a treatment system aims to provide very high-quality soft tissue imaging for guidance before and during treatment delivery.[15–22] Low- and high-field MR imaging systems have been used thus far,; with a linac or three cobalt sources mounted on a slip-ring gantry structure as the radiation delivery system. An alternative solution has been an MR system on rails, which can be moved into the vicinity of the linac in the treatment room.[23]	*Prostate T2w 3D image.* 
Ultrasound	The use of high-frequency sound (ultrasound) for acquiring images of internal structures in or around the target volume. Ultrasound images are acquired at pretreatment within the CT simulation suite and registered with the planning CT image and/or the radiotherapy (RT) generated structure sets. The position of the transducer can be linked either optically or mechanically to a detection system that relates its position to the treatment room isocentre.[24,25]	*Ultrasound images for prostate.* 

Ultrasound does not use ionising radiation. It visualises internal structures around the target volume and with respect to OAR. Imaging can be compromised unless there is an appropriate 'acoustic window' for the ultrasound waves to penetrate the body (ie, minimal bony obstructions are required between the skin's surface and the target volumes).[26] Also the pressure of the ultrasound probe can sometimes deform underlying tissues thereby giving false image information for the situation during actual treatment delivery.[27,28]

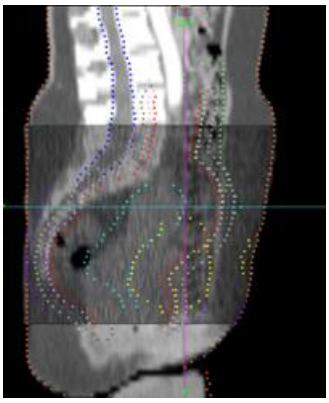
MVCT

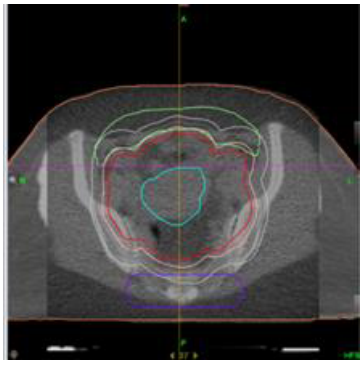
There are two methods of acquiring MVCT.

- 1. Tomotherapy – a modality of X-ray radiation therapy that combines the use of a linear accelerator, multi-leaf collimator (MLC) and high-efficiency CT detector. The MV energy fan beam creates a volumetric image for verification with helical scanning as used in conventional CT imaging.[29] Scan length is flexible but large length requires long scan times, which will affect throughput and potentially allow time for organ motion.
- 2. Units where the treatment beam line is used in combination with a flat-panel detector to acquire CT.

Generally provides poorer image quality than kV-based methods but may be advantageous for patients with high-density implants.[6,30]

MVCT overlay with planning CT.





4.3 Four-dimensional imaging and tracking

Four-dimensional (4D) imaging refers to imaging of the target before the delivery of radiotherapy to quantify target motion. The latter can be used to enable treatment when a target is in the appropriate place (gating), track motion (tracking) or interrupt treatment in case the target is out of tolerance (exception gating). 4D on-treatment imaging may come with a cost in acquisition time, dose, storage and complexity of analysis. It should therefore preferably only be used in situations where 3D or 2D imaging techniques are insufficient.

Breath-hold can be used as an alternative method of compensating for respiratory motion and has been investigated in lung cancer and abdominal tumours.[31] A deep-inspiration breath-hold (DIBH) is the generally accepted methodology to increase distance between the heart and the breast and has been reported as well tolerated and reproducible for patients with breast cancer.[32,33] However, the reproducibility of breath-hold must be verified, interfraction and intrafraction and also interbreath-hold and intrabreath-hold.[34] Note that if a breath-hold treatment is used, a 4D CT scan is not an appropriate reference because the inhale phase during breathing is generally not representative for a breath-hold. (Neither the inhale nor exhale phases of the 4D CT represent inhale and exhale breath-hold.) In the latter case a 3D CT acquired with the identical breath-hold procedure should be used as reference.

4.3.1 Image acquisition and review for 4D image guidance

The most commonly used 3D imaging technologies, including CBCT, work on the assumption that the tumour is static during image acquisition. Therefore any movement (for example, thoracic-induced respiratory motion) will cause 'blurring' and/or artefacts in the reconstructed image.

Therefore, when imaging tumours in the lung or abdomen in free breathing, particularly if close to the diaphragm, this blurring may affect the apparent size, shape and location of the tumour. This makes decision-making more difficult when performing online treatment verification corrections. According to Rit *et al*, tumour motion of over 1 cm peak to peak reduces accuracy of 3D CBCT-based guidance and therefore 4D imaging strategies are required.[35]

4D imaging on the treatment machine

The term 4D imaging relates to adding time or phase information to 3D imaging. The most common method of 4D imaging is 4D CBCT. MRI, ultrasound, surface-based imaging, planar imaging of markers and implanted transponders have also been used to obtain 4D information. Many of these techniques add the time element to non-volumetric imaging and therefore they are not true 4D, but they will still be considered in this section.

4.3.2 Reference images for 4D verification

The most common reference image for 4D verification would be derived from the 4D planning CT scan. This scan is acquired by sorting slices according to a respiratory sensor such as a belt or an optical sensor. Irregular breathing during 4D CT acquisition leads to image artefacts.[36] Patients should be given enough time to relax before starting acquisition, as observed using the respiration signal. It is important that radiographers are trained in this process. Also the order of image acquisition may be important – for example, undertaking the most important part of the scan last.

Most IGRT systems require a 3D reference image. Great care should be taken that this reference image matches the (average) situation during treatment or that if there is a difference this is incorporated by using appropriate margins, which can be asymmetric – for instance, when an exhale image is used as reference to verify free-breathing treatment. When treatment is performed gated in exhale, the exhale frame of the 4D CT image loop would be the most appropriate reference image. For treatment in free breathing, one can use the average CT, maximum intensity projection (MIP), a selected phase or a mid-position CT scan as reference.[37,38] Both the average CT and MIP are suboptimal reference images because the tumour will show with blurring in this image that is not present in the 4D image. However, if 3D CBCT image guidance is used the average of the 4D CT would be the most appropriate reference as it should have equivalent blurring.

Note that if image guidance is performed directly on the tumour (as in SABR treatments) and the plan is made on the same image used as reference for IGRT, no error would be introduced in the position of the tumour itself whatever the reference image is. However, the relative position of tumour and OAR could be incorrect. This means that, in the absence of 4D CT, a fast free-breathing 3D CT scan could be used as a reference image (where the tumour motion is captured in a fraction of one breathing phase) as long as appropriate planning risk volumes (PRVs) are used with the OAR. In this case 4D CBCT could be used to verify tumour motion.

Other requirements for reference images in 4D workflows are identical to 3D workflows (see the previous section).

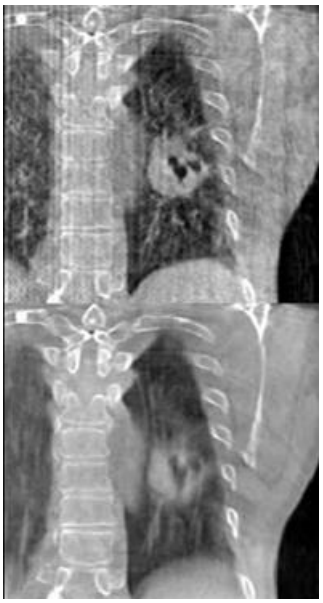
4.3.3 Acquisition modes for 4D image guidance

Table 3 shows acquisition modes for ionising radiation-based 4D image guidance. Other methods are described below.

Table 3. Acquisition modes for ionising radiation-based 4D image guidance

Technique	Description	Example
4D CBCT	4D CBCT acquisition commonly sorts the projection images into the correct breathing state to provide a movie-loop-style visualisation of respiratory motion.[39] 4D CBCT requires more projections and thus a longer scan time compared with conventional CBCT. Scan times down to two minutes are, however, used clinically. When using the same exposure per projection image, 4D CBCT requires a higher dose than the corresponding 3D CBCT due to the longer acquisition time. However, the increased imaging artefacts due to undersampling in each 4D CBCT frame may have a more deleterious	*Comparison of a 4D CBCT frame (top) and a 3D CBCT (bottom). Due to undersampling, the 4D CBCT has streaking artefacts that show in this view as vertical lines.*

effect on image quality than quantum noise, so in general there is no loss of information when 3D CBCT and 4D CBCT are acquired with the same dose – for example, for 4D CBCT the exposure per projection image could be halved if the scan time is doubled.[40]

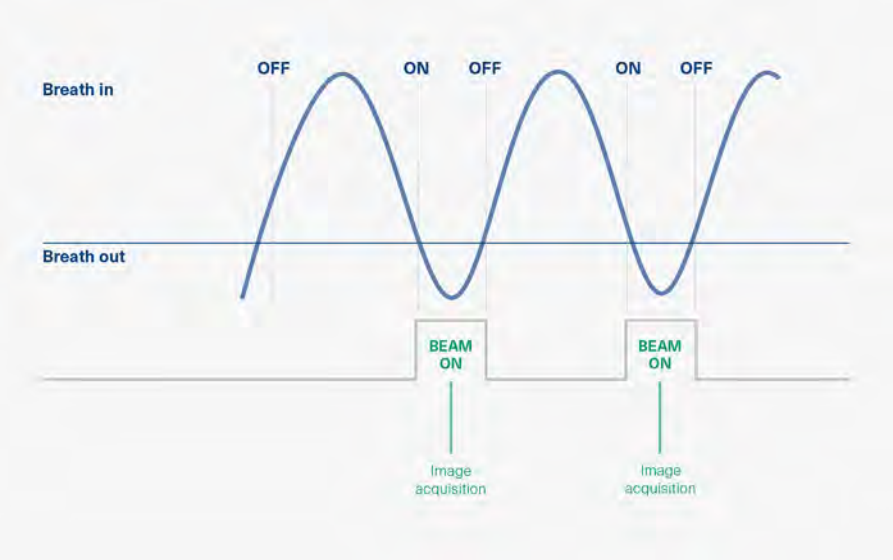


Gated imaging

Prospective gated imaging requires measuring a breathing surrogate signal to trigger imaging only when the surrogate is in a predefined state. The advantage of gating image acquisition is that only the most 'useful' images are acquired to assess breathing trajectories, which could reduce patient imaging dose.[41] This is an important consideration moving forward in 4D/tracking implementation.

With treatment delivery, the 4D system can be implemented to interrupt the treatment beam when respiratory motion is outside accepted tolerances and resumed when respiration motion is back within tolerance. The intended result would mean more precision in the delivery of radiotherapy to mobile tumours by ensuring adequate target coverage and minimising the chance of a geometric miss. It is important to note that external anatomy does not always correlate with internal motion and therefore the correspondence must regularly be verified by imaging.[42]

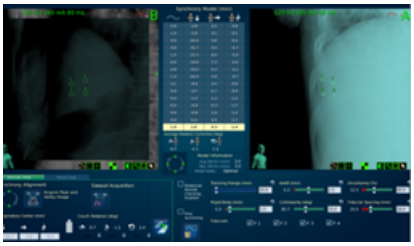
Treatment delivery synchronised with a window in the breathing cycle.



Imaging for tracking

Tracking requires continuous updating of the beam delivery system to the motion of the target. To localise the tumour or its surrogate, continuous or intermittent imaging is used. In the latter case, a motion model is maintained and updated that predicts the tumour location from a surrogate signal. Currently, most tracking systems are based on kV imaging. MRI, ultrasound and transponder-based systems are discussed below.

Static image of CyberKnife user interface, demonstrating kV imaging of implanted fiducials to guide tumour tracking.



4.4 Fiducial marker-based tracking methods

Fiducial markers can be used to facilitate motion measurement and image guidance. It may be necessary for markers to be implanted in or near the tumour or tumour bed to get the most appropriate surrogate for target position (for example, prostate, liver or pancreas).[43] They should not be placed in close proximity to bony landmarks due to reduced visibility and potential restriction of their motion.

4.4.1 Image acquisition and review

There are two styles of fiducial markers. The most common one acts as an indicator of an anatomical structure, in that it adds additional contrast so the structure can be readily localised on the imaging method of choice. Various IGRT systems provide manual or automatic methods to localise fiducial markers. The second style of marker uses optical or electromagnetic signals such that it can be localised in real time without imaging, through dedicated hardware and software.

4.4.2 Reference images

Internal fiducial markers are implanted before CT scanning and a delay should be planned between implantation and CT scanning to let any procedure-induced potential swelling subside (see Section 5). The size and material of the imaging markers should be compatible with the imaging procedure used to obtain reference and verification images.

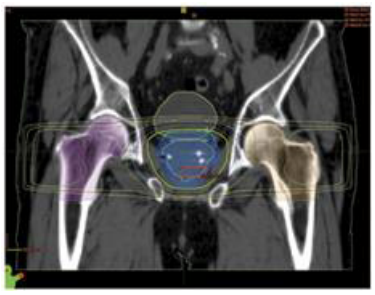
External fiducial markers should be visible on the reference images.

Note that fiducial markers can cause imaging artefacts that can degrade the quality of the image and may affect target volume delineation and registration (see Section 5.1).

4.4.3 Acquisition modes for fiducial marker-based tracking methods

Table 4 describes the different types of markers used.

Table 4. Fiducial markers

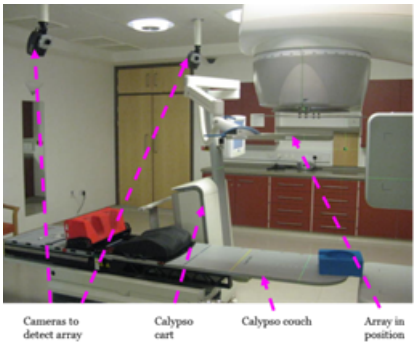
Technique	Description	Example
Fiducial markers	Radio-opaque fiducial markers are easy to visualise on 2D or 3D imaging. They can either provide additional information on the images acquired (eg, CBCT for prostate cancer) or be used as a surrogate for target position in planar imaging where soft tissue information is not available. Radio-opaque fiducial markers visible on fluoroscopic imaging can be used to automatically track or gate the treatment.	*Coronal planning CT showing three gold fiducial markers within the prostate.*[44] 
External fiducials	External fiducials are markers attached to the external anatomy (eg, markers on the patient surface or in the external frames). They are typically detected with optical tracking and may be used where external motion is a good surrogate for internal motion or as a surrogate respiration signal.[45]	*External markers on frames.*  

Implanted transponders

These systems allow for real-time, continuous monitoring during treatment delivery by means of beacon (wireless) transponders implanted in the tissue close to the target volume. Implantation is similar to that used for fiducial markers for X-ray-based systems.[46]

Transponders are implanted before CT scanning and their positions noted with respect to the isocentre of the treatment plan.

On-treatment tracking using the Calypso system.



4.5 Patient surface-guided IGRT approaches

Surface-guided radiotherapy is the use of external surrogates (the patient's external anatomy).

The available systems typically do not involve ionising radiation to monitor the patient and therefore can help initial set-up and provide real-time intrafraction monitoring.

However, because of the poor correlation between external surface and internal anatomy in many cases, surface-based approaches are not a replacement for other forms of IGRT.

4.5.1 Image acquisition and review

There are a number of commercially available solutions for surface-guided IGRT and these can be used in combination with other forms of IGRT to monitor patient position during treatment delivery and to facilitate gating or breath-hold techniques.

4.5.2 Reference images for surface tracking

It is crucial that the same surface-guided approach is applied at pretreatment/initial CT simulation and then throughout the patient's radiotherapy treatment delivery.

4.5.3 Acquisition modes for patient surface-guided IGRT approaches

Table 5 describes methods for surface tracking.

Table 5. Methods for surface tracking

Technique	Description	Sample image
Surface methods	These systems allow for a continuous monitoring of the patient's surface in real time, quickly and with no concomitant dose burden.[47–50,28] Surface tracking uses photogrammetry, using light and light patterns projected or scanned onto the patient's surface.[48,50–56] The relationship between the external markers or the skin surface to the target volume structures must be determined through pretreatment scanning and planning; geometric verification is evaluated through this assumption or with respect to information taken in the treatment room with additional imaging (planar or volumetric). The methods allow for the possibility of gating treatments (turning off the treatment beam if geometric errors are outside a predefined tolerance) during continuous monitoring of patient position, and even for verifying the correct patient identification.[57]	 

Recommendations

- Good-quality images are essential and treatment image quality should ideally have adequate spatial resolution to visualise the structures of interest with sufficient contrast-to-noise ratio.
- 2D acquisition methods should be optimised to produce the quality required.
- 3D volumetric techniques should be considered where possible because of improved contrast and for analysis and visual verification.
- Manufacturer-supplied 3D acquisition presets should be adapted to suit individual departmental requirements.
- 4D on-treatment imaging should preferably only be used in situations where 3D or 2D imaging techniques are insufficient because of the cost in acquisition time, dose, storage and complexity of analysis.
- Care should be taken when using a 3D reference image for a 4D treatment image. The reference image should match the (average) situation during treatment or if there is a difference be incorporated by using appropriate margins, which can be asymmetric.
- Fiducial markers should be implanted in or near the tumour or tumour bed.

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5. Verification process

5.1 Pretreatment process

The pretreatment process defines the baseline anatomy on which the treatment plan is generated for IGRT. Therefore, patient position and anatomy should be as close as possible for daily treatment to the pretreatment imaging with the same immobilisation and motion management techniques employed. Patient comfort is essential to maintain reproducibility and immobilisation systems need not be overly complex. Immobilsation equipment is a key component of accurate radiotherapy delivery and must be considered as part of routine equipment replacement programmes.

If fiducials are used, potential migration should be considered, which typically occurs in the first few days after implantation, requiring the minimum wait between insertion and planning CT to be predefined. Fiducials can cause image artefacts that may hamper image interpretation and are a surrogate for target volume. In addition, not all of the target volume may be mobile relative to the markers (for example, seminal vesicles versus prostate markers) and this may require bigger margins and/or volumetric guidance to ensure coverage.[1]

The planning scan should cover all regions receiving treatment dose and extend to the full coverage of OAR that have volume constraints. For instance, the mean lung dose is widely used as a constraint – this can only be calculated correctly if the full lungs are covered in the scan.[2] In contrast, since the most widely used constraint for the spinal cord is a maximum dose, the scan does not need to be extended to cover it all but does need to include all of the spine where it may receive a clinically significant radiation dose.[3]

The scan should have a suitable image quality (pixel size, slice distance, signal-to-noise ratio) to be able to accurately define the target and relevant OAR.[4] If the patient's anatomy moves significantly during (3D) image acquisition, for instance due to respiration, deformation is introduced and 4D imaging is warranted and should be used. In case of involuntary motion, a scan may need to be repeated.

For the purpose of this report, the most important use of the pretreatment scan is as a reference for IGRT. This means that patient preparation and image acquisition should be comparable with the online image. For instance, if significant amounts of contrast (oral and/or intravenous [IV]) are used in a planning CT and not in the online imaging, this might confuse automatic registration of IGRT systems. This can be solved by using diluted contrast or by excluding the contrast from the ROI.

Another example is where 3D CBCT is used for verification of lung cancer therapy and the scan shows an effective average anatomy. This is comparable with an average-intensity projection (AIP) of a 4D CT scan. Therefore the use of an MIP reference image could create a mismatch in anatomical information and lead to inaccuracies when matching to the 3D CBCT image.[5]

In case 4D verification is used, a 'sharp' reference image is required, this may be obtained with techniques such as mid-ventilation.[6] Note that if multiple CT sequences are acquired, it is essential that the CT series used as reference is identical to the one used for planning.

Most verification systems can display planning contours. It is useful to decide which contours should be visualised and would enhance the image interpretation. Equally, it should be considered that additional structures could confuse matching and prevent visualisation/prioritisation of relevant structures. If particular contours can be generated that enhance the image guidance or adaptive process (selected isodose lines for critical

structures), these should be named appropriately and consistently, as nomenclature is essential in selecting the correct structure.[7] This issue is even more important in the case of plan selection, where several sets of contours are made available. These contours are often used to create or form ROI for image registration. Typically such ROI should be slightly bigger than the target (to provide image contrast) but exclude nearby structures with differential motion (for example, pelvic bone for prostate or ribs for lung tumours).

In cases where a non-CT IGRT system is used (for example, ultrasound, MRI or surface-guided radiation therapy (SGRT)) it is good practice to use the same modality as reference image. Great care should be taken to avoid anatomical mismatch between this reference image and plan. Connectivity issues are covered in Section 3.

Recommendations

- Patient position and anatomy should be reproducible at daily treatment, using the same preparation, immobilisation and motion management.
- Patient comfort is essential to maintain reproducibility.
- Fiducials are a surrogate for target volume but may not represent the full motion of the target volume.
- Reference scan extent should include all regions receiving treatment dose and extend to the full coverage of OAR that have volume constraints.
- Suitable image quality (pixel size, slice distance, contrast-to-noise ratio) is required to ensure accurate definition of the target and relevant OAR.
- Patient preparation and image acquisition should be consistent with that of the online images.
- It is essential that the CT series used as reference is identical to, or intrinsically linked with, the CT used for planning.
- Relevant contours that enhance the match should be made visible and any additional structures that could confuse matching should be omitted.

5.2 Treatment image analysis (online, intrafraction and offline)

The structure outlined below has been chosen to complement the site-specific guidance in Section 10.

Once a localisation image has been acquired, it must be evaluated for mismatch with the reference image and then be analysed to derive appropriate correction. This may simply be a table shift and/or rotations, or may highlight the need for adaptation (for example, replanning). The timing and frequency of the imaging depends on the treatment plan/intent, the treatment technique and the type of correction strategy (offline, online or intrafraction). There is a shift towards more online verification, likely due to the better tools that are available (for example, automated table shifts), the procedure becoming more routine and it being simpler because it does not require any information from previous fractions.

Overall, IGRT processes are now more streamlined. Offline protocols, which can reduce on-set resources, may be used depending on accuracy requirements. In these cases it is essential to adhere to appropriate correction strategies, where ad hoc imaging and correction have little or no impact on treatment accuracy. Nowadays, even if an offline

protocol is used, with imaging on selected fractions, online correction can be performed for those fractions. On non-imaging fractions the correction derived from the uncorrected set-up error measured on one or more previous fractions needs to be used.

For efficiency, the online registration and correction process should, where possible, be performed by radiographers involved in the actual patient set-up. However, the radiographers should also be trained and competent (see Section 9) to interpret the localisation images for anatomical changes that affect the position or stability of the tumour and/or OAR or the accuracy of dose delivery. It is also imperative to detect changes that may be related to medical conditions (for example, lung collapse) and take appropriate action, such as warning the clinician or delaying treatment. It should be noted that without appropriate competency, typically more cases would be referred to the clinician, delaying the process and affecting workflow and accuracy (for example, organ motion increases with time).[8] Appropriate quality control of the registration process should be performed. This may capture errors that have been made, ensuring these cases are learned from. A good example is bony alignment on the wrong vertebrae. An independent second check in particular for high-dose hypofractionated regimes (for example, SABR) is strongly recommended, but ideally should be done for standard fractionation regimes as this can reduce the chance of errors. The amount of checking should be compatible with the clinical goal and should not compromise workflow. Note that some clinical trials have mandated second checking. In addition, it is recommended to have an audit process in place, for instance checking random images for image quality and quality of analysis.

Modern IGRT systems have automated registration algorithms. The performance of these algorithms depends critically on their settings. In particular, the ROI should be chosen with great care to be representative of the target or OAR and exclude high-contrast anatomy with differential motion to the target. In all cases, automatic algorithms can fail, so the results should always be checked visually. It is good practice to prospectively define IGRT protocols that include such settings in detail. This saves time, improves consistency and reduces the chance of errors. Note that often there is differential motion between the target and OAR (for example, lung SABR and spinal cord). This may lead to violation of OAR dose constraints just by setting up the target accurately. In such cases, it is advised to localise both the target and OAR and evaluate the impact of their differential motion. If necessary, treatment can be deferred or target coverage can be compromised to keep the OAR dose within acceptable limits.

Where intrafraction monitoring is used, appropriate thresholds should be set so that only clinically relevant motion leads to treatment interruption – in other words, that would lead to unacceptable target underdose or OAR overdose, taking into account whether it is a fractionated/hypofractionated treatment. Processes to correct for intrafraction motion are not well developed. One possibility is to wait until the motion has resolved (for example, passing gas in prostate cancer treatment). It is possible to shift the table but that can lead to interplay effects away from the target that moved. Dose accumulation software to evaluate these effects is available but in many cases not accurate enough to be used in clinical practice due to the poor handling of sliding tissue.

Localisation images should be acquired under the same conditions as treatment.[9] This is particularly important if gating or tracking is used, or treatment is performed under breath-hold. In cases where surrogates are used for gating or tracking, it is essential to check the correlation of such structures with relevant internal anatomy, for instance using volumetric or planar (if the tumour is visible) imaging.

5.3 Post-treatment imaging

Post-treatment imaging is a useful tool to estimate intrafraction motion and residual error. It is particularly useful for hypofractionated radiotherapy regimes (for example, SABR) because the impact of intrafraction motion tends to be greater given the longer duration of treatment fractions, the smaller number of total fractions and the smaller margins typically used in SABR. This or another intrafraction monitoring technique should be used when introducing new radiotherapy techniques or changing existing techniques (for example, a change in immobilisation device).

A limitation of post-treatment imaging is that intrafraction motion may not be fully captured. In practice, however, imaging post-treatment may overestimate this motion because the images of the situation prior to and after treatment will be compared. The observed differences will therefore be representative of a longer time period than the actual treatment.

5.4 Rotations

The typical magnitude of rotations of bony anatomy is around one degree standard deviation (SD).[10] Rotations of the prostate itself can be extreme, with an SD of around five degrees around the left–right axis.[11] Such rotations have been measured using three implanted markers.

The impact of rotations, however, depends on the shape of the target.

- **Example 1:** as the prostate is almost spherical, its rotations have hardly any influence on prostate coverage and therefore should not be corrected. Note that these rotations would also move the attachment points of the seminal vesicles. However, because the seminal vesicles are mobile there is little correlation between prostate rotation and seminal vesicle motion.[11] The situation may be different when boosting a part of the prostate, since typically the boost region is in the periphery of the prostate and therefore moves with rotations. Correction of bone rotations is of benefit when treating prostate and pelvic lymph nodes simultaneously due to the elongated shape of the target.[12]
- **Example 2:** rotations of the skull are not likely to be relevant when treating a single target with semi-spherical shape. However, when treating multiple brain metastases with a single isocentre, rotations become more important depending on the distances between the different targets. In general, the best location of the isocentre is at the centre of gravity of the multiple targets, where less important targets may be weighted less. Because of the geometry, if there are two metastases at 57 mm from the isocentre (for example 114 mm apart), one degree rotation corresponds with 1 mm displacement of both targets relative to the isocentre – that is, two degrees SD of rotation corresponds with a 2 mm SD of displacement of the targets. Such a displacement will have both a random and systematic component.

When the target region in the online image is rotated compared with the same region in the reference image it is difficult to get a proper alignment with translations only because there will always be a shape misfit. This means that the algorithm will have difficulty finding the correct registration, and that the operators will have a difficult task validating the registration. If the IGRT solution allows it, it is therefore preferred to enable rotations for image registration even if there is no intention to correct for them.

Rotations in a 6D registration are generally defined around the isocentre and the order in which they are applied is system dependent. Zeroing rotations after registration to derive a table shift will therefore correctly position the isocentre but can significantly move organs that rotate. For example, if the prostate has rotated 11 degrees and is registered including rotations (for instance, using fiducial markers) and it is 2 cm from the isocentre, after zeroing rotations the prostate will be mispositioned by about 4 mm {sin(11°) x 20 mm}. If an off-centre target is treated that may rotate, rotations should therefore be executed around the centre of the target. In some IGRT systems a secondary centre of rotation can be defined to alleviate this problem. If this is not possible, use of off-centre treatments should be avoided or registrations should be performed without rotations.

The effect of rotations on treatment is generally small, because most targets are relatively round. Be aware, however, that rotations may affect locations of OAR as well.

Tilt and roll couches exist that can correct rotation up to three degrees. Such corrections may induce secondary organ motion (up to 0.6 mm per degree has been reported), depending on the direction of rotations, body site and immobilisation.[13] In general, patients should be aggressively immobilised when rotating the couch. Do not try to rotate the couch to correct prostate rotations as they are very big and not of relevance. Be aware that if only part of the rotation is corrected only the isocentre will be in the right place and large errors can be induced for structures away from the isocentre, as explained above for rotation of the prostate. It is therefore important to know how the system works and to design protocols that are safe given the potential limitations. It should be noted that in many cases, correction of rotations can cause more problems than it solves.

Rotations can be reduced by immobilisation; for example, aggressive immobilisation such as a fixed bite block can eliminate most rotations of the head.[14] Even though five-point masks were designed to reduce rotations they are not particularly effective. Proper use of an individualised neck rest is likely to be more effective in reducing rotations.[15] For the pelvic area, leg, knee and foot immobilisation are known to be effective to reduce rotations.[16] Aligning patients straight and in line with the centre of the couch can be helpful. It is important that rotation during CT simulation is reproduced on the treatment machine. The patient therefore has to be CT scanned in a reproducible and comfortable position.

Recommendations

- For efficiency, the online registration and correction process should, where possible, be performed by radiographers involved in the actual patient set-up.
- It is essential that changes related to medical conditions are detected and reported appropriately, to ensure suitable action.
- An audit process should be in place to ensure good quality of images and analysis standards.
- The ROI for matching should be representative of the target or OAR, excluding high-contrast anatomy with differential motion to the target.
- Ideally prospectively defined IGRT analysis protocols should be used.

- Where differential motion exists, it is advised to localise both target and OAR to evaluate the impact.
- Surrogates used for gating or tracking should be correlated to relevant internal anatomy, for instance using volumetric or planar (if the tumour is visible) imaging.
- It is important to know how the system deals with rotations and to ensure that no error in the target position is induced by not using correction rotations or only using them partially.

5.5 Dose considerations and concomitant exposure

Concomitant exposures are defined as all exposures within the course of radiotherapy other than treatment exposures and are mostly commonly associated with imaging acquired throughout the patient pathway. The Ionising Radiation (Medical Exposure) Regulations (IR(ME)R) 2017/2018 require that *all* medical exposures to ionising radiation are justified and optimised.[17,18] This means that the benefits of imaging (such as improved target definition or treatment accuracy) should outweigh the potential risks associated with the concomitant dose that will be delivered to the patient. Dose optimisation can also be a consideration to choose between online and offline IGRT strategies and the number of images used.[19]

While associated radiation doses should be kept ALARP, it is important to ensure that this is done without compromising the image quality that is required to perform the clinical task (for example, planning treatments and contouring relevant organs in the scan volume or verification of patient set-up prior to treatment). Note that a 'good-quality' image is one that is suitable for the clinical task and this may not be the best possible image attainable. Importantly, a good-quality image for one task may not be appropriate for another.[18,20]

Within IR(ME)R, the following roles are defined,interpreted here in the context of IGRT.

Referrer: must be a registered healthcare professional. The referrer is entitled to refer individuals requiring exposure to a practitioner in accordance with the employer's procedures and is required to provide sufficient clinical information to enable the practitioner to make a decision about justifying the medical exposure. In an IGRT context this refers to any extra imaging that delivers additional ionising radiation to the patient.

Practitioner: must be a registered healthcare professional. The practitioner's primary role is justifying and authorising concomitant imaging exposures.

Operator: does not have to be a registered healthcare professional but needs to be a trained individual. The operator can carry out practical aspects relating to exposure and is individually responsible for all practical aspects of the procedure they undertake. In an IGRT context the operator performs the imaging and is responsible for the practical aspects of radiation exposure.

Medical physics expert: gives advice on dosimetry and QA matters. The medical physics expert (MPE) contributes to the optimisation of image quality and radiation protection of patients and other individuals subject to exposures. They also contribute to the analysis of events involving, or potentially involving, accidental or unintended exposures.

Given the complexities of modern radiotherapy treatments, it is important that IR(ME)R practitioners consider the whole patient pathway when justifying concomitant imaging exposures. It should always be remembered that the primary aim of radiotherapy is to deliver accurately a high dose of radiation to a target volume, while minimising the exposure of surrounding organs; if imaging helps in this process it should be used. It should be recognised that higher-dose imaging protocols *may* result in a net dose saving to healthy tissue if improved image quality results in better target localisation or accuracy of treatment delivery, which in turn should lead to better patient outcomes.

This observation does not negate the requirement to optimise all exposures under IR(ME) R. In addition, the most appropriate imaging modality should be used. For example, the additional dose required for a 4D CT planning scan can be justified if it allows more accurate delineation of moving targets. When 4D CT allows better determination of peripheral lung tumour motion during respiration, it ensures more accurate treatment and potentially margin reduction and associated reduced normal tissue exposure. However, it is likely not justified where tumours and OAR are located in stable anatomy.

Specific consideration should also be given to the benefits of CBCT imaging over planar X-ray techniques and the most appropriate technique used. Even though CBCT imaging will always yield more clinical information, this may not translate into greater treatment accuracy so, in a limited number of cases, planar X-ray imaging can still be justified (for example, for short-course palliative treatments). Uncertainties in the evaluation process may instigate a change in imaging protocol (for example, 3D imaging will be preferred if the 2D imaging does not provide sufficient image detail).

It is a legal requirement that doses for the full range of imaging protocols are characterised and made available to the referrer. Practitioners will also need to be fully aware of these doses to justify the exposure. The choice of dose parameters should be carefully selected when comparing imaging and radiotherapy exposures. Effective dose is a common descriptor used in imaging to quantify the risk associated with exposures to a typical, 'healthy' population. This may be of some use in the justification process (especially if evaluating the risk of secondary cancer far from the treatment field) but in radiotherapy it is usually organ doses that are of most interest. It may therefore be more useful to quantify imaging dose in a similar way to assess the potential impact on the treatment and any possible side-effects. 3D and 4D CBCT dose is reported as ranging from approximately 1–5 cGy per scan.[21,22] Over the course of treatment under a daily imaging protocol, this may result in total organ doses of 1–3% of the prescribed dose, meaning absolute doses in excess of 1 Gy for high-dose imaging protocols.[18] However, if this additional dose enables a similar or greater reduction in radiotherapy dose to the same organ, this is easily justified. It may also be acceptable in situations where there are no net dose savings to the patient, provided there are other clear benefits such as improved targeting of treatments, improved safety or the ability to treat sites that would be impossible without imaging. In cases such as this, the imaging dose should be considered in the treatment planning process if it exceeds 5% of the prescribed dose.[22]

The onus is on individual centres to verify that the imaging protocols provided with new equipment are suitable for the clinical tasks to which they will be applied and to modify them if necessary. It is particularly important to consider if the protocols provided on the equipment fully encompass the range of patients and work performed in the centre. Often, systems are configured with a single protocol for a limited range of anatomical sites; this is most likely not optimised for all clinical sites encountered by individual centres and

consideration should be given to developing local protocols that allow adaptation to the size of the patient wherever possible. It is advised to organise such protocols by tumour site to provide flexibility of optimisation and ease of use. It is often the case that vendor default settings will deliver doses that are much higher than required on paediatric and smaller patients (image quality much greater than required for the clinical task), while image quality may not be acceptable on larger, bariatric patients (dose may be too low in these cases). As this work is extensive, it is strongly encouraged that centres with similar equipment build on each other's expertise. Local and national dose reference levels need to be established. The updating of reference levels through involvement in audits, both regional and UK-wide, is encouraged. National dose reference levels for CT planning scans have been published on the Public Health England (PHE) national diagnostic reference levels (DRLs) website and values for CBCT verification imaging are to follow.[23]

The expected number and dose of concomitant exposures, including scope for repeat imaging where required, should be included within site-specific protocols. These should include clear guidance on where imaging is justified by the IR(ME)R practitioner, detail specific imaging protocols that should be used and provide authorisation criteria that enable the IR(ME)R operators to perform the required imaging.

Provision for anticipated repeat imaging can be included in imaging protocols to allow prompt decisions and repeat imaging when appropriate. The requirement to repeat imaging due to operator, procedural or equipment errors should be subject to individual incident investigations as detailed in the IR(ME)R guidance.[17,18,24]

In the case of an accidental or unintended exposure the referrer, practitioner and individual exposed (or their representative) must be informed when discovered. All need to be informed of the outcome of the investigation as recorded and reported in line with the recommendations in *Ionising Radiation (Medical Exposure) Regulations: implications for clinical practice in radiotherapy* produced by the Radiotherapy Board.[25] The practitioner, or another suitable clinician, should follow the duty of candour legislation to ensure that providers are open and transparent. Duty of candour regulations apply as soon as reasonably practicable after a safety incident has occurred.[26]

Therefore, for all cases, it is important to ensure clear and accurate record-keeping (most often in the electronic oncology information system) of all imaging events alongside the treatment parameters; this must include the exposure factors used (these may be recorded automatically with the image data). Audit of repeat imaging is helpful in monitoring imaging performance and optimising exposure protocols (akin to reject analysis in diagnostic imaging). Repeat imaging audits allow trends to be identified that may require remedial action; for example, a high number of repeats due to image quality concerns should prompt a review of protocol settings, while a high number due to bowel status may prompt a review of bowel preparation guidance given to patients.

Under IR(ME)R the optimisation process should closely involve an MPE and it is highly recommended that an MPE with specific training and expertise in diagnostic imaging should work as part of the wider clinical team (including, for example, other physicists, radiographers and clinicians). Alongside a consideration of dose, image quality in relation to the clinical task should be evaluated. The concept of image quality in IGRT covers both geometric accuracy and ability to interpret and act appropriately on that image. The quality and reconstruction of the initial planning CT will potentially influence the initial contouring for treatment planning, TPS dose calculations and the accuracy of the IGRT matching

process for treatment. A balance is required to ensure that the quality of the planning scan is sufficient for all applications to which it is being applied. Similarly all verification images should be of sufficient quality so as not to deteriorate this accuracy.

To assist in the optimisation process, a collaborative approach between the diagnostic and radiotherapy communities should be promoted within individual centres. This should enable the sharing of relevant experience to allow:

- Dose quantification, across all modalities, with a common language
- Optimisation of the images for the intended purpose
- Understanding of common image artefacts and avoidance methods
- Establishment of an appropriate QA programme (as required under IR(ME)R), with awareness of the system's performance and tolerance limits.

Imaging protocols should be reviewed regularly by an appropriate multidisciplinary team (MDT), including trained operators. As techniques and available image-guidance technologies change over time, it is also vital to assess that the imaging protocols remain fit for purpose and the concomitant dose trade-off is taken under consideration. Alternative image-guidance methodologies that do not require radiation exposure should also be considered.

In summary, the concomitant dose from image guidance, which may be significant, should be offset by the increased accuracy of treatment, provided these exposures have been effectively optimised.

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6. Geometric uncertainties

6.1 Geometric error definitions

The term 'geometric error' is used in this document to describe any discrepancy between intended and actual treatment position. With the exception of gross errors, it includes a systematic and random component.

With the increase in daily online imaging strategies, the set-up error component becomes less dominant and other sources of error should be investigated and accounted for. Delineation error is an example, where incorrect delineation will cause systematic errors to be introduced to the treatment pathway, which may go undetected. Further definitions are detailed below.

Note that the organisation of this document does not match the new British Institute of Radiology (BIR) report *Geometric uncertainties in daily online IGRT*, which focuses on the measurement of the magnitudes of components of uncertainty.[1] In this report we consider the clinical impact of each source of uncertainty and explicitly consider the random and systematic uncertainties separately. References to BIR terminology are provided.

6.1.1 Gross error

A gross error is a large unacceptable set-up error that would result in an extreme underdose of the CTV or an extreme overdose to OAR. Treatment margins are not intended to account for gross errors, therefore gross errors must be detected and corrected before treatment commences. Statistically, gross errors would be outliers in the distribution of errors.

Gross error must be determined by one of the following methods.

- Acquire and review pretreatment images immediately before treatment delivery. These images will be used to verify correct patient site and orientation, laterality, isocentre position, patient contour and internal anatomy. Where a gross error is detected, the cause of it must be ascertained and corrected before continuing treatment.
- As above, using the first treatment unit session for verification alone (day 0). This should be used where a complex set-up or a large dose per fraction is being delivered.
- Where a beam arrangement cannot be accurately visualised on imaging, gross error can be investigated by reviewing the light field in relation to surface anatomy. This is often used for electron or skin treatments and vertex fields.

Possible causes of gross error include:[2]

- Incorrect patient, anatomical site or patient orientation
- Incorrect field size, shape or orientation
- Incorrect isocentre position
- Gross change in anatomy
- Incomplete target definition.

6.1.2 Systematic error

The systematic component of any error is a deviation that occurs throughout the treatment course. It is typically estimated by averaging errors measured during multiple fractions.

When considering geometric uncertainties in radiotherapy, the term systematic error may be used when referring to the individual patient or to the treatment population; this distinction should be clarified to avoid confusion.

- **Individual:** the systematic error for an individual patient is the mean error over the course of treatment.
- **Population:** the systematic error for a group of patients is an indication of the spread of individual mean errors. Its uncertainty is calculated as the SD of the distribution of mean errors for each individual patient and is given the capital sigma symbol Σ_{error} where the subscript 'error' refers to the particular error considered (for example, $\Sigma_{set\text{-}up}$ for the measured systematic set-up error). There will also be a population mean error; where this is small ($<0.4\Sigma$) it may be ignored.[1]

Most systematic errors are introduced into a patient's treatment at localisation or planning. For this reason these types of errors are often referred to as treatment preparation errors.[3] Once introduced, systematic errors will occur in each treatment fraction. Possible systematic errors are summarised below.[1]

- **Target delineation error (BIR: delineation error):** this is introduced when the GTV/CTV is first delineated and represents a difference between the defined and 'ideal' CTV. As a result of the fact that online daily imaging reduces systematic and random errors on treatment and target delineation errors are typically not corrected, they become the dominant portion of the overall error. Departments should implement standardised delineation protocols to reduce the likelihood of gross delineation errors. Peer review is recommended to provide QA in delineation of target volumes across different treatment sites.[4] The introduction of different image modalities into the contouring stage to aid in target delineation will result in some error associated with image fusion[5] (BIR: matching error).[1] Gross errors in delineation should be identified with QA, while smaller errors should be evaluated and included in the treatment margin calculation.[1,6–8]
- **Patient set-up error:** this describes a misposition of the overall patient anatomy (as reflected by the position of the bony anatomy) between planning and treatment. This error is typically corrected by IGRT, although a part of this systematic error may remain if offline correction is used. Also if few fractions are used, intrafraction motion may have a non-negligible residual component.[1]
- **Target position, shape and rotational errors (BIR: target deformation, rotational errors and surrogate errors):** this is a change in target position, shape and rotation between delineation and treatment. Possible causes include tumour regression or growth or effects of the filling of hollow organs on adjacent tumours. Without ART such errors are either not corrected or only partially so. If a surrogate is used to set up a target, the relative motion of a surrogate (for example, an implanted marker) and the target is described by the BIR surrogate error. Motion between the target and the bony anatomy is a form of surrogate error. If the target moves quickly (for example, due to respiration or heartbeat), a fast planning scan acquisition would freeze this motion in an arbitrary position, introducing a systematic error. In this case, 4D acquisition may be appropriate and post-processing (average, selection or motion compensation) may be used to create a representative scan that minimises this systematic error.[9]

- **Intrafraction motion:** if few fractions are delivered the error introduced by motion between imaging for image guidance and treatment (see below) may not average out and a residual systematic error is introduced.
- **IGRT observer variability (BIR: matching error):** this is the variation that will occur with varying observers performing analyses of the same IGRT data set and should be quantified locally. Consistent training and competency will help to reduce this, as will adherence to local and national protocols and ongoing peer review (see Section 9). These errors will mostly average out over many fractions, but can be an important source of systematic error for hypofractionated regimes. The accuracy of automatic image registration depends for a large part on the quality of the used images and used settings, which are vendor specific. Development of site-specific image guidance protocols including, for instance, regions of interest can help to minimise the latter uncertainty.
- **Technical IGRT accuracy limitations (BIR: technical delivery accuracy):** this describes the residual uncertainty of the IGRT system and linear accelerator. Centres should be aware of the limitations of their systems and how these can affect patient set-up. Sources of IGRT localisation error are: inconsistency of linac and imaging equipment isocentre, accuracy of the system to implement couch moves and accuracy of the position of beam-limiting devices (MLC). Most of these uncertainties are addressed by machine QA, in which case their magnitude is defined by the acceptance tolerances.[10,11] These errors are classed as systematic because their causes either do not change (image resolution, margin algorithm) or are assumed to vary slowly (isocentre position, leaf position accuracy) and are therefore taken as constant over the typical treatment duration.

6.1.3 Random error

The random component of any error that varies for each delivered treatment fraction.

The term 'random error' may be used to refer to the individual patient or to the treatment population and, as for systematic errors, this distinction needs to be clarified to avoid confusion.

- **Individual:** the random error for an individual patient is the SD of the measured errors over the course of treatment and quantifies the spread of errors.
- **Population:** the random error for a group of patients is calculated as the root mean square (RMS) of the individual random errors and is given the lower case sigma symbol σ_{error} where the subscript 'error' refers to the particular error considered (for example, $\sigma_{set\text{-}up}$ for the measured random set-up error).

Random errors occur at the treatment delivery stage and, for this reason, are often referred to as treatment (or daily) execution errors.[3] They are summarised below.

- **Patient set-up error:** these are varying, unpredictable changes in a patient's position (described by the bony anatomy) between each delivered fraction.[12] Intrafraction patient motion is considered below.
- **Target position, shape and rotational errors (BIR: target deformation, rotational errors and surrogate errors):** the change in target position, shape and rotation between fractions. For some tumour sites, bony anatomy is a reliable and accurate surrogate for the tumour position. Many tumours can, however, move, rotate and

deform independently due to internal organ motion.[13] To achieve optimum treatment accuracy it is essential to be able to visualise the tumour itself or insert a marker in or near the tumour if possible. This error is essentially the same as that described above for systematic errors but accounts for motion between fractions rather than from delineation to treatment.

- **IGRT observer variation:** as described previously for systematic errors but for every fraction.
- **Intrafraction errors:** this describes changes in the patient's position and internal anatomy arising during the delivery of any single fraction (for example, due to breathing or motion of the target between localisation and treatment). This error can also have systematic components (for example, due to patient relaxation). Post-treatment imaging can quantify both intrafraction motion and residual errors to a certain extent, but has limitations on how much information is accrued throughout the treatment itself.[14] If evaluated for a population the data can be used to verify the PTV margin for that protocol. Intrafraction errors can otherwise be measured by imaging during treatment.[15]

Random errors are influenced by the immobilisation system, patient compliance and department protocols. If a new immobilisation device is introduced, it is likely that the random error will be affected. An offline correction strategy cannot predict the random error component in subsequent fractions and so treatment margins must be calculated to include these sources of error. Online correction strategies are needed to correct random errors, but it should be realised that the impact of random error is much smaller than the impact of systematic errors.[16]

6.2 Geometric error measurement

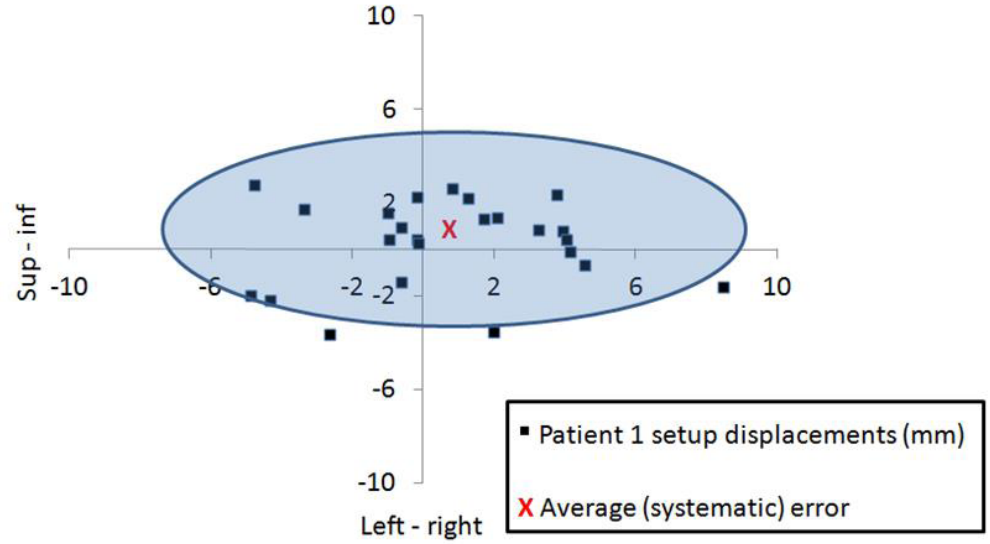
The error measured from a single image will contain both systematic and random components. As outlined above, the systematic part of the measurement will nominally be constant from one fraction to the next whereas the random part will vary in an unpredictable way.

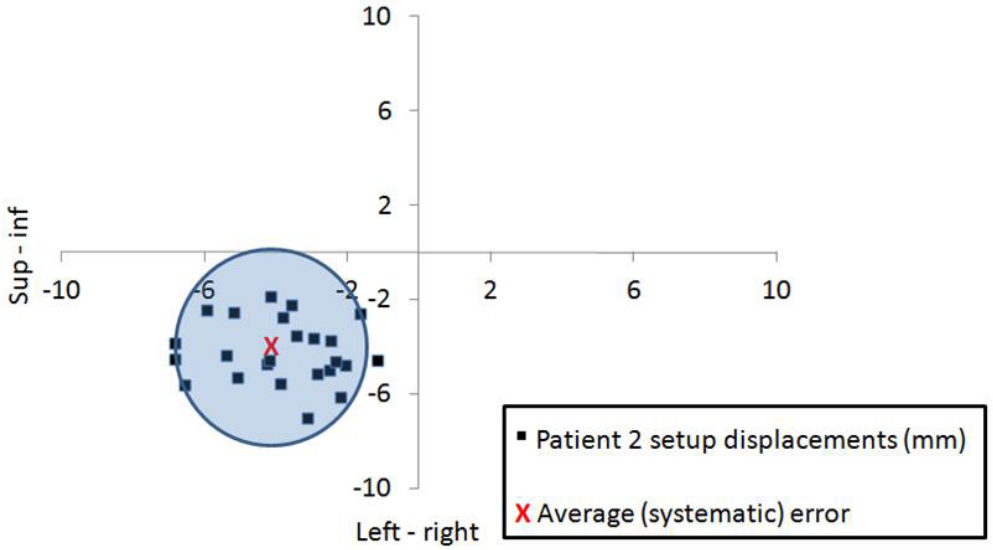
The difference between systematic and random error is demonstrated in Figure 5, where the daily treatment verification data have been plotted for two patients. The information shows that each patient has different systematic and random errors occurring during their treatment; Patient 1 has a small systematic error but larger random errors, while Patient 2 has a larger systematic error but smaller random errors. These examples also demonstrate that more than one image must be acquired to distinguish between the systematic and random components and provide a good 'estimate' of any correction to be applied, especially where daily online imaging cannot be used. Offline actions based on a single image must be undertaken with caution as they can lead to magnification of errors. For example, if the image of Patient 1 associated with the set-up error of 8 mm right and 5 mm inferior was used in isolation to correct subsequent treatments, a considerable overcorrection would be made. Further images taken and acted on independently would also be subject to the same outcome, leading to a series of unnecessary corrections around the mean position. For this reason, most offline imaging correction strategies acquire images over the first few fractions to provide a more accurate estimate of the mean.[17,18]

Ideally, all departments should determine their own population systematic and random set-up error components for each site-specific group.

Figure 5. Difference between systematic and random errors

Daily set-up errors (in mm) from anterior/posterior images acquired for two patients over the course of treatment. Patient 1 exhibits a small systematic (mean) set-up error compared with Patient 2. Patient 1 has a larger, random spread of errors. Although Patient 1 has an overall treatment accuracy close to that intended, any individual image taken is a poor indicator of this mean position. Therefore data from multiple (minimum of three) images should be combined when used for offline correction.





6.3 Geometric errors and treatment margin

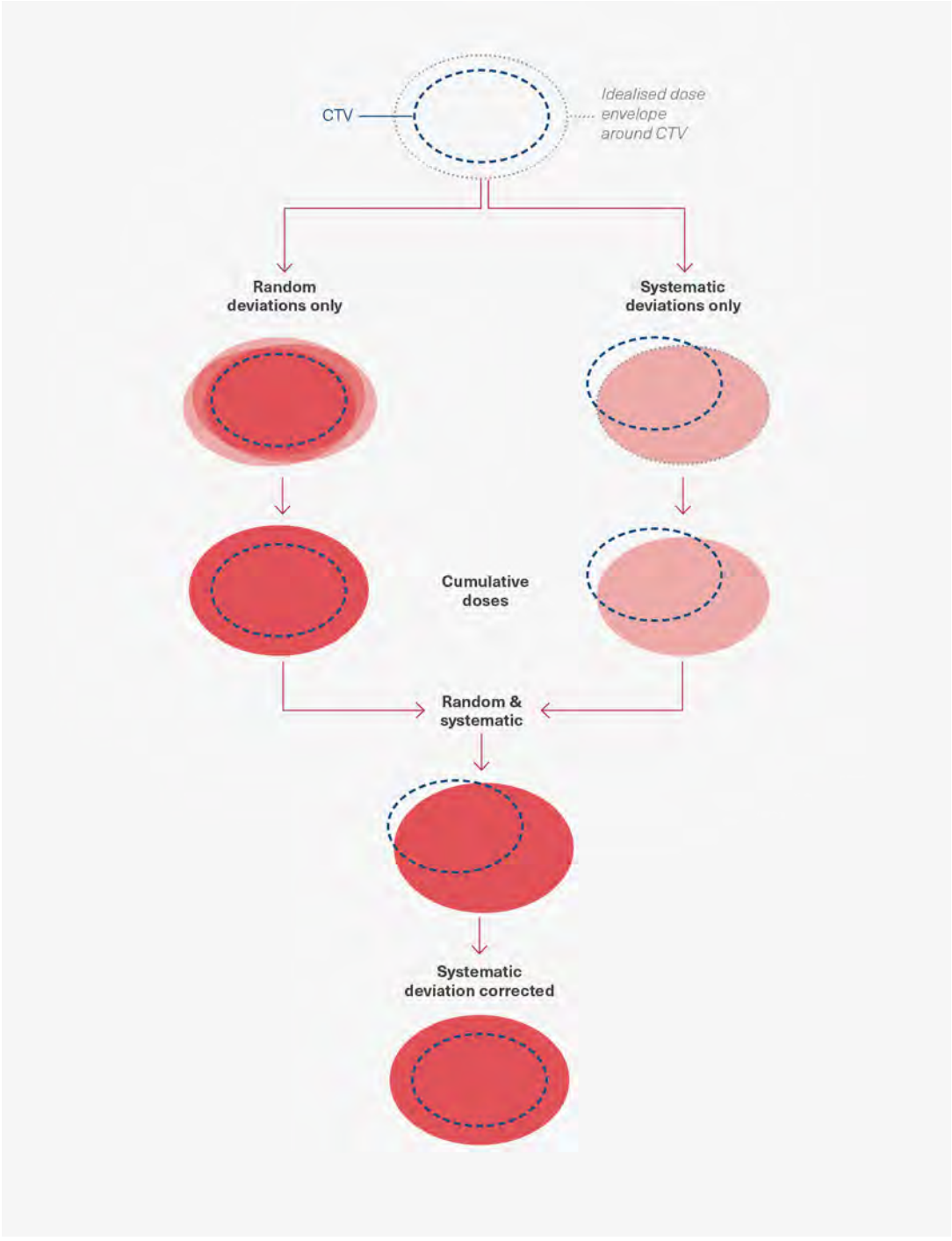
Geometric errors and CTV-PTV margins are interlinked. Figure 6 shows the impact of systematic and random errors on CTV coverage. It demonstrates that random errors, which vary from day to day, lead to a blurring of the cumulative dose distribution around the CTV, whereas systematic errors could lead to too low a cumulative dose to a portion of the CTV. Because of this latter effect, most of the CTV-PTV margin is needed to ensure adequate coverage from the various sources of systematic error. Systematic errors have a larger dosimetric impact on the CTV than random errors and must therefore be the focus. The CTV-PTV margin may be modified depending on the number of contributing errors that can be detected and corrected during the course of treatment. This will be dependent on the treatment verification method used and which contributing error can be imaged. These may be summarised as follows:

Offline imaging of bony anatomy	Aims to correct systematic patient set-up errors including phantom transfer errors.
Offline imaging of target	Aims to correct systematic errors associated with target position and shape that can occur between delineation and first treatment.
Online imaging of bony anatomy	Aims to correct systematic and random patient set-up errors.
Online imaging of target	Aims to correct random and systematic errors associated with target position. Note that even after online imaging of the target there are residual errors (eg, related to system accuracy, changes of shape of the target and intrafraction motion).

Although online and offline imaging measure the same parameters, an online approach measures the error before treatment and enables correction of the total error for that treatment; that is, systematic plus that day's random errors. With online correction the accuracy of the registration and the limitations of the equipment (for example, couch movement) become more significant. Each individual department must evaluate its equipment and any other potential sources of error. The department should then base its actions on the resulting data.[19] Margins can be used from established protocols (such as national and local guidance or research protocols) but each radiotherapy department should still evaluate its own uncertainties for each treatment site and technique to ensure these margins are appropriate.

The target delineation error cannot be measured for an individual patient and is present for the treatment course. As mentioned above, gross delineation errors should be avoided and remaining delineation uncertainty should be incorporated into the CTV-PTV treatment margin. A practical method to estimate delineation uncertainty is outlined in the worked example.

Figure 6. The impact of geometric deviations on the dose distribution relative to the CTV



Random (treatment execution) deviations lead to a blurring of the dose distribution. Systematic (treatment preparation) deviations lead to an unknown shift in the cumulative dose distribution relative to the CTV.[3] An offline correction strategy aims to quantify and correct for the systematic errors occurring over a course of treatment, so that mostly random errors remain.

Recommendations

- Gross errors should be detected, their cause investigated and corrected once understood.
- Systematic errors have a larger dosimetric impact on the CTV than random errors and must therefore be the focus.
- To establish appropriate CTV-PTV margins, sources of error other than patient set-up errors should be quantified, such as delineation uncertainties.
- Margins can be used from established protocols (such as national and local guidance or research protocols) but each radiotherapy department should still evaluate its own uncertainties for each treatment site and technique to ensure these margins are appropriate.

6.4 Tolerances and action levels

6.4.1 Tolerances

The 'tolerance' of any measurement or parameter may be defined as the permitted observed variation in that measurement or parameter. Tolerances are defined to trade off accuracy versus workload and clinical gain. For instance, measured patient rotations (if not corrected) may be given a tolerance of a certain number of degrees before the patient needs to be set up again. Such tolerance values should be determined for each treatment site and protocol.

6.4.2 Action levels

An action level for a measurement or parameter is the point at which action is necessary, typically as part of a correction protocol. In an offline protocol, action levels are set such that the resulting systematic error is within tolerance based on measurement of a fixed or variable number of fractions.[1,17,18]

The action to be taken depends on the importance of the parameter, the risk of not making any alteration and the workload. Where online image review is used, anything exceeding the action level should be corrected. For most systems, automatic couch corrections are performed and verification imaging after correction is not necessary, provided that the system has been appropriately quality assured and the action of the table motion does not cause displacement of the patient. A series of action levels may be set whereby, for a small deviation from the tolerance, observation is recommended. For a larger deviation, immediate amendment is required to compensate. However, for deviations outside a preset level (a gross error) a fresh set-up and/or reimaging may be required. It is important to always investigate the source of such gross errors prior to the decision to treat.

Action levels can also be applied for observed variations in anatomy away from the target or its surrogate (for example, due to deformations or weight loss). These are discussed in further detail in Section 7 (adaptive radiotherapy).

Recommendations

- Since there is no or little workload and minimal uncertainty associated with automated patient set-up corrections, it is recommended to use no action thresholds for daily table corrections.
- Gross errors should always be investigated.
- Action levels can also be applied for more complex corrections, such as adaptive replanning for deformations or weight loss.

6.5 Derivation of systematic and random errors and relationship to the CTV-PTV margin

The remainder of this chapter describes:

- How the random and systematic errors for a group of patients may be derived
- Calculation of CTV-PTV margins.

An example is presented to demonstrate the method, illustrating margin calculation for the most commonly used online protocols. For offline protocols refer to Section 14 (Appendix 14.1).

6.5.1 Error

The error (Δ) is defined as the deviation between actual and expected position, normally calculated as a shift in the isocentric position when an image is compared against its corresponding reference. Classically the term 'set-up error' is used to describe motion of the bony anatomy relative to the treatment machine. However, in this document references to 'error' mean the motion of a particular anatomical region relative to the treatment machine. Conversion of measurements into the required co-ordinate axes may be made if the acquired images are not orthogonal.[20,21] It is crucial that vector quantities are calculated so the correct direction information is maintained. For example, if shifts in the anterior direction are given a negative sign then those in the posterior direction are always positive. The equations used to calculate these are given below and split into two basic forms: those calculating a mean and those calculating an SD. The SD is a measure of how widely values are dispersed from the mean value and in this context defines the size of the error.

The term 'treatment population' is used to represent all patients treated with a specific technique (treatment site and immobilisation method). The errors for this population are estimated by calculating the errors for a group of patients whose results are assumed to accurately represent those of the population from which they are drawn.

6.5.2 Systematic errors

Individual mean error

The systematic error ($m_{individual}$) is the mean error for an individual patient. It is calculated by summing the measured error for each imaged fraction ($\Delta_1 + \Delta_2 + \Delta_3 ...$) then dividing by the number of imaged fractions (n). This can be expressed by the formula:

$$m_{individual} = \frac{\Delta_1 + \Delta_2 + \Delta_3 + \ldots + \Delta_n}{n}$$

(E1)

Overall population mean error

The overall mean error (M_{pop}) is the overall mean for the analysed patient group and should ideally be zero. Significant departures from zero indicate an underlying error common to this patient group, requiring investigation. This parameter is a strong indicator of the efficacy of any given treatment technique and is often omitted. The equation is essentially the same as equation 1 with the means for each individual patient (m_1, m_2, m_3...) now being summed and the total divided by the number of patients in the analysed group (P).

$$M_{pop} = \frac{m_1 + m_2 + m_3 + \ldots + m_P}{P} \quad \text{(E2)}$$

Population systematic error

The systematic error for the population ($\sum_{set\text{-}up}$) is defined as the SD (spread) of the individual mean errors around the overall population mean (M_{pop}). It is calculated by summing the squares of the differences between the overall population mean derived from equation 2 and each individual patient mean derived from equation 1 in turn.

Note that the resultant sum is divided by the number of patients minus one and the square root of the resultant value is required to calculate $\sum$.

$$\Sigma^2_{set\text{-}up} = \frac{(m_1 - M_{pop})^2 + (m_2 - M_{pop})^2 + (m_3 - M_{pop})^2 + \ldots + (m_n - M_{pop})^2}{P - 1} \quad \text{(E3)}$$

6.5.3 Random errors

Individual random error

For each individual, the interfractional random (daily) error ($\sigma_{individual}$) is the SD of the set-up errors around the corresponding mean individual value (m) derived from equation 1. It is calculated by summing the squares of the differences between the mean and error from each image in turn. Note that the resultant sum is divided by the number of images minus one and that the square root of the resultant value is required to give $\sigma_{individual}$.

$$\sigma^2_{individual} = \frac{(\Delta_1 - m)^2 + (\Delta_2 - m)^2 + (\Delta_3 - m)^2 + \ldots + (\Delta_n - m)^2}{n - 1} \quad \text{(E4)}$$

Population random error

The population random error ($\sigma_{set\text{-}up}$) is calculated as the RMS of all the individual random errors (σ_1, σ_2, σ_3....). This equation assumes that the number of images acquired per patient is identical or that the likely differences will have minimal effect on the final result.

$$\sigma^2_{set\text{-}up} = \frac{\sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \ldots + \sigma_P^2}{P} \quad \text{(E5)}$$

6.6 Margin derivation

It is beyond the scope of this document to discuss the derivation and calculation of CTV-PTV margins in detail. Several population-based margin calculation recipes have been proposed.[3,22,23] These address the differences between random and systematic errors and how they are to be combined to produce an appropriate margin. Most of these margin calculation recipes can be expressed as follows:

$$\mathrm{CTV}-\mathrm{PTV}_{\mathrm{margin}} = a\Sigma + b\sigma \tag{E6}$$

where Σ and σ are the combined sum of the SDs of all contributing systematic and random errors respectively, and **a** and **b** are constants. The two constants **a** and **b** characterise the relative contributions of the systematic and random components, and these depend on factors such as the beam arrangement and chosen coverage probability.[3,22] Typically **a** is 3–4 times greater than **b** and Σ is often larger than σ, indicating that the key contributor to the margin is the combined systematic error.[23] Figure 6 demonstrates the relative effects that systematic and random errors have on the cumulative dose to the CTV.

The combined systematic error includes all possible sources of error. The SDs of these five contributing sources ($\Sigma_{\mathrm{delineation}}$ = target delineation, Σ_{target} = target position, shape and rotation, $\Sigma_{\mathrm{intrafraction}}$ = residual systematic intrafraction motion, Σ_{IGRT} = IGRT accuracy, and $\Sigma_{\mathrm{technical}}$ = machine accuracy) are assumed to be normally distributed and independent of each other, and may be combined in quadrature (equation 7) to produce the combined systematic error Σ. There is some work suggesting that $\Sigma_{\mathrm{delineation}}$ may require handling in a different way than the other components and needs an alternate theoretical approach.[24] For the purposes of the analysis below, the total error is assumed to be normally distributed, which is a reasonable assumption given the central limit theorem, which states that the distribution of a sum of an increasing number of errors with an arbitrary distribution will tend towards normal:

$$\Sigma^2 = \Sigma^2_{\mathrm{delineation}} + \Sigma^2_{\mathrm{target}} + \Sigma^2_{\mathrm{intrafraction}} + \Sigma^2_{\mathrm{IGRT}} + \Sigma^2_{\mathrm{technical}} \tag{E7}$$

The components contributing to the combined random error are σ_{target} and σ_{IGRT} and $\sigma_{\mathrm{intrafraction}}$ where σ_{target} is the random target error (including random surrogate error and random variation in organ position and shape), σ_{IGRT} is the random error introduced by the IGRT system and observer and $\sigma_{\mathrm{intrafraction}}$ is the SD of intrafraction motion. These two components can also be combined in quadrature in a similar manner to equation 7 to give the combined treatment execution error σ.

It can be seen that imaging studies will provide important input data to the margin calculation for both the random and systematic components. Note that breathing motion has not been covered explicitly in the margin calculation. According to clinical evidence in current literature it can be included identically to other motion contributions.[25] In clinical practice, however, many centres will use an internal target volume (ITV) approach, meaning that breathing motion is added linearly, which leads to somewhat excessive margins.[9]

Caution should be applied when implementing the results of a margin calculation clinically. Where some uncertainties have not been included, the margin may become too small and clinical results affected.[26] For this reason, departments that change margins should carefully monitor their results.

Recommendations

- Margins must take into account all elements of uncertainty.
- With IGRT in place, the residual margin will be determined by those parts of the random and systematic errors that are left uncorrected.
- The magnitude of the CTV-PTV margin is largely governed by the combined systematic (treatment preparation) errors.

6.6.1 Worked example (online strategy)

A worked example for an online strategy of margin derivation for prostate and seminal vesicles is presented here in Tables 6 to 10. For a worked example of an offline strategy, refer to Section 14 (Appendix 14.1). All measurements are in centimetres. The data were collected by analysing repeat CT scans of patients with prostate cancer. First the bony anatomy of the planning CT and 11 scans was registered and from this position the motion of the anatomy was measured by grey value registration of two regions of interest, the prostate and a seminal vesicle. The data were analysed in Kershaw *et al*.[27] Because there is relative motion of different parts of the anatomy, the required margin depends on what structure is used for IGRT, and margins are not zero, even for daily online guidance. In the analysis, the planning CT is included, which by definition has a zero error (as it is the reference). This is a recognised approach to avoid a bias due to the limited number of measurements.

Figure 7. Analysis of set-up error of the prostate for the worked example

A) Collection of 12 repeat CT scans registered on bony anatomy. B) The same scans after registration on the prostate. In particular in fraction 2, a large shift and rotation is visible. For the subsequent analysis the motion of the centre of gravity of the different regions was analysed.

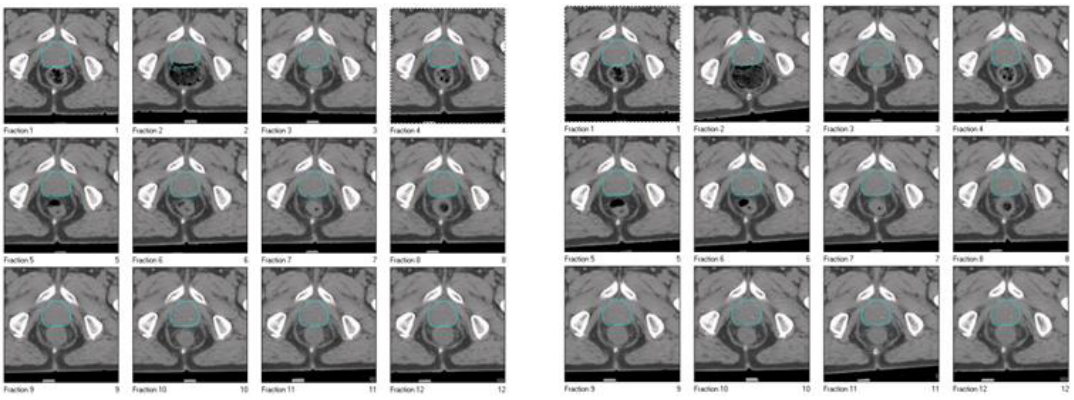


Table 6. Individual set-up errors of prostate (P) and right seminal vesicle (SVR)

Data in cm, acquired from a single patient measured in repeat CT for 11 fractions along the three anatomical axes (LR, SI, AP), using the method shown in Figure 7. Prior to measuring the organ motion, the bony anatomy was registered; that is, these motions are relevant for set-up correction on bony anatomy. The lower two rows give the individual patient mean and SD. Rows that are highlighted appear in follow-up tables.

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Bone protocol	Planning CT	0.00	0.00	0.00	0.00	0.00	0.00
	Fraction 1	0.08	0.23	0.63	−0.21	0.42	1.02
	Fraction 2	0.05	0.05	0.00	0.03	−0.07	−0.07
	Fraction 3	−0.01	0.07	−0.05	−0.04	0.04	−0.05
	Fraction 4	−0.05	0.09	0.18	−0.17	0.16	0.32
	Fraction 5	−0.06	0.11	0.01	−0.19	0.12	0.10
	Fraction 6	−0.04	0.10	0.06	−0.13	0.07	0.09
	Fraction 7	0.00	0.16	0.01	−0.02	0.19	0.05
	Fraction 8	−0.07	0.26	−0.03	−0.12	0.27	0.01
	Fraction 9	−0.03	0.00	−0.22	−0.06	−0.10	−0.27
	Fraction 10	−0.04	0.28	0.09	−0.13	0.53	0.37
	Fraction 11	0.02	0.33	−0.09	−0.04	0.35	−0.04
	Mean	**−0.01**	**0.14**	**0.05**	**−0.09**	**0.17**	**0.13**
	SD	**0.04**	**0.11**	**0.21**	**0.08**	**0.20**	**0.33**

Table 7. Individual set-up errors of prostate (P) and right seminal vesicle (SVR)

Data in cm, acquired from a single patient measured in repeat CT for 11 fractions along the three anatomical axes (LR, SI, AP). Prior to measuring the organ motion, the prostate was registered; that is, these motions are relevant for set-up correction on prostate. The lower two rows give the individual patient mean and SD. Even though it is assumed prostate motion is perfectly corrected, there is residual motion of the SV. Similarly, there will be residual motion for lymph node regions and similar.

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Prostate protocol	Planning CT	0.00	0.00	0.00	0.00	0.00	0.00
	Fraction 1	0.00	0.00	0.00	−0.29	0.19	0.39
	Fraction 2	0.00	0.00	0.00	−0.02	−0.12	−0.07
	Fraction 3	0.00	0.00	0.00	−0.04	−0.03	0.00
	Fraction 4	0.00	0.00	0.00	−0.12	0.08	0.14
	Fraction 5	0.00	0.00	0.00	−0.13	0.01	0.10
	Fraction 6	0.00	0.00	0.00	−0.08	−0.03	0.03
	Fraction 7	0.00	0.00	0.00	−0.02	0.03	0.04
	Fraction 8	0.00	0.00	0.00	−0.04	0.01	0.04
	Fraction 9	0.00	0.00	0.00	−0.03	−0.10	−0.05
	Fraction 10	0.00	0.00	0.00	−0.09	0.25	0.28
	Fraction 11	0.00	0.00	0.00	−0.06	0.02	0.05
	Mean	**0.00**	**0.00**	**0.00**	**−0.08**	**0.03**	**0.08**
	SD	**0.00**	**0.00**	**0.00**	**0.08**	**0.11**	**0.13**

Table 8. Individual mean and random set-up errors for three patients

With similar data as in Tables 6 and 7 derived using equations 1 and 4. Assuming perfect correction for prostate, its mean and SD goes to zero, but for all patients there is residual motion of the SV. To calculate representative motion statistics, data of 16 additional patients were used, but these are not shown for brevity.

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Bone protocol	Mean 1	−0.01	0.14	0.05	−0.09	0.17	0.13
	Mean 2	0.01	−0.09	−0.10	0.02	−0.25	−0.14
	Mean 3	0.03	−0.22	−0.24	−0.06	−0.45	−0.22
	(Data for patients 4–19 not shown)						
	Mean	0.00	−0.05	−0.07	−0.02	−0.02	−0.03
	SD	0.04	0.15	0.23	0.10	0.27	0.29

	SD 1	0.04	0.11	0.21	0.08	0.20	0.33
	SD 2	0.07	0.15	0.19	0.05	0.25	0.22
	SD 3	0.06	0.19	0.21	0.05	0.35	0.33
	(Data for patients 4–19 not shown)						
	RMS	0.05	0.20	0.23	0.09	0.27	0.30
Prostate protocol	Mean 1	0.00	0.00	0.00	−0.08	0.03	0.08
	Mean 2	0.00	0.00	0.00	−0.04	0.16	0.16
	Mean 3	0.00	0.00	0.00	0.01	−0.16	−0.05
	(Data for patients 4–19 not shown)						
	Mean	0.00	0.00	0.00	−0.02	0.03	0.03
	SD	0.00	0.00	0.00	0.08	0.19	0.12
	SD 1	0.00	0.00	0.00	0.08	0.11	0.13
	SD 2	0.00	0.00	0.00	0.05	0.18	0.15
	SD 3	0.00	0.00	0.00	0.08	0.22	0.12
	(Data for patients 4–19 not shown)						
	RMS	0.00	0.00	0.00	0.09	0.18	0.13

Table 9. Resultant population systematic and random set-up errors in each orthogonal direction

Using equations 3 and 5 for a 19-patient group, including the three patients in Table 8. Data are given with bone and prostate based set-up correction.

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Bone protocol	M_{target}	0.00	−0.05	−0.07	−0.02	−0.02	−0.03
	Σ_{target}	0.04	0.15	0.23	0.10	0.27	0.29
	σ_{target}	0.05	0.20	0.23	0.09	0.27	0.30
Prostate protocol	M_{target}	0.00	0.00	0.00	−0.02	0.03	0.03
	Σ_{target}	0.00	0.00	0.00	0.08	0.19	0.12
	σ_{target}	0.00	0.00	0.00	0.09	0.18	0.13

When calculating the appropriate safety margin for a treatment based, for instance, on a prostate set-up error correction protocol, it is not sufficient to use the data from Table 9. Error sources that are not included in this table are delineation uncertainty, observer variation in the image guidance process, intrafraction motion in the time between set-up error correction and treatment delivery and technical accuracy limitations of the equipment. Figure 8 shows an example of delineation variation, where ten observers outlined the prostate. Table 10 shows a more complete margin calculation including these uncertainties.

Figure 8. Estimation of observer variation in prostate delineation

Ten observers outlined the prostate, but obviously there are some interpretation differences. These should be solved by changing (make clearer) the delineation protocol, and are not measured here as observer variation. The SD of the observer variation is estimated for the representative spread of contours (measured close to perpendicular to the prostate surface) divided by a factor of ~3 for ten observers.[1] Here the range is 0.66 cm, estimating an SD of 0.22 cm. Ignoring outliers around the SV, the SD is similar to the prostate body.

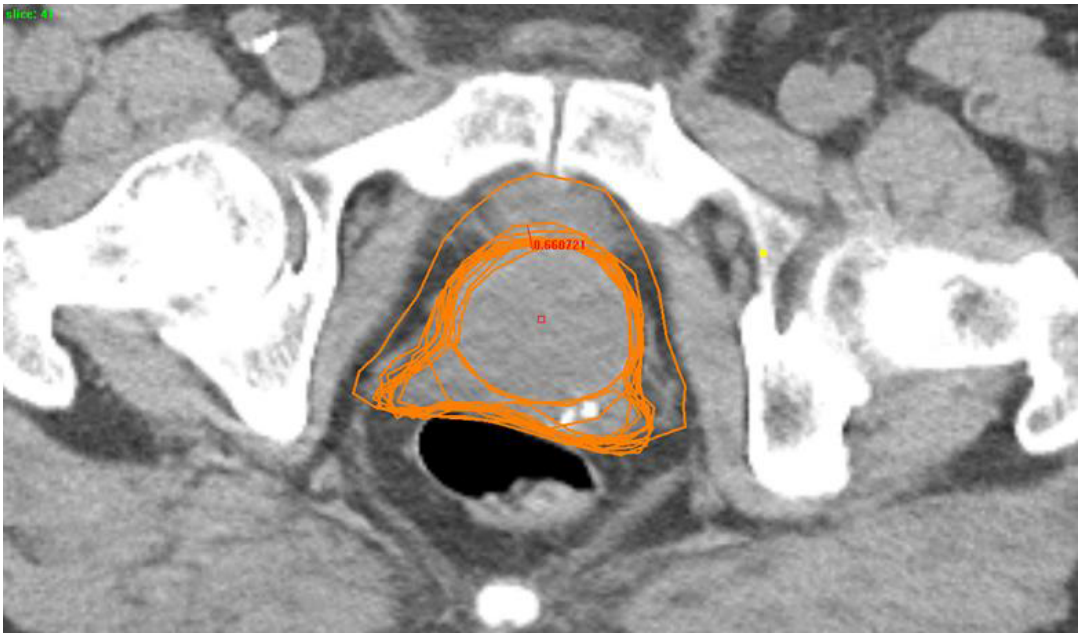


Table 10. Margin estimation for prostate and SV for bone and prostate-based set-up correction, taking into account delineation variation and assuming SD=0.1 cm as intrafraction motion

In this derivation the prostate is assumed to be perfectly spherical and non-deformable such that rotational errors and deformation errors are zero. Technical errors are taken as maximum 0.1 cm, SD 0.03 cm. The IGRT registration error for bone is assumed to be 0.01 cm, for prostate 0.2 cm (which is representative for a soft-tissue set-up on CBCT).[28,29] Over 25 fractions these reduce by a factor of five. Table 10.1 shows the margin calculation for a bony anatomy set-up protocol, while Table 10.2 shows a prostate (soft tissue) protocol. Note that organ motion is bigger for the bone protocol, but the IGRT error smaller.

Table 10.1. Bone-based set-up protocol

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Bone protocol	$\Sigma_{delineation}$	0.22	0.22	0.22	0.22	0.22	0.22
	Σ_{target}	0.04	0.15	0.23	0.1	0.27	0.29
	$\Sigma_{intrafraction}$	0.02	0.02	0.02	0.02	0.02	0.02
	Σ_{IGRT}	0.002	0.002	0.002	0.002	0.002	0.002
	$\Sigma_{technical}$	0.03	0.03	0.03	0.03	0.03	0.03
	Σ_{total}	0.23	0.27	0.32	0.24	0.35	0.37
	σ_{target}	0.05	0.2	0.23	0.09	0.27	0.3
	σ_{IGRT}	0.01	0.01	0.01	0.01	0.01	0.01
	$\sigma_{intrafraction}$	0.1	0.1	0.1	0.1	0.1	0.1
	σ_{total}	0.11	0.22	0.25	0.13	0.29	0.32
	Margin	**0.64**	**0.83**	**0.98**	**0.71**	**1.08**	**1.14**

Table 10.2. Prostate-based set-up protocol

		P_LR	P_SI	P_AP	SVR_LR	SVR_SI	SVR_AP
Prostate protocol	$\Sigma_{delineation}$	0.22	0.22	0.22	0.22	0.22	0.22
	Σ_{target}	0	0	0	0.08	0.19	0.12
	$\Sigma_{intrafraction}$	0.02	0.02	0.02	0.02	0.02	0.02
	Σ_{IGRT}	0.04	0.04	0.04	0.04	0.04	0.04
	$\Sigma_{technical}$	0.03	0.03	0.03	0.03	0.03	0.03
	Σ_{total}	0.23	0.23	0.23	0.24	0.3	0.26
	σ_{target}	0	0	0	0.09	0.18	0.13
	σ_{IGRT}	0.2	0.2	0.2	0.2	0.2	0.2
	$\sigma_{intra\text{-}fraction}$	0.1	0.1	0.1	0.1	0.1	0.1
	σ_{total}	0.22	0.22	0.22	0.24	0.29	0.26
	Margin	**0.73**	**0.73**	**0.73**	**0.77**	**0.95**	**0.83**

6.6.2 Comments on the example

It is obvious that derivation of treatment margins incurs significant effort. It may therefore be reasonable to use literature data, but it should be checked that these are relevant for the clinic. Organ motion data have been shown to be fairly consistent, but this motion does depend on patient preparation (for example, for bowel and bladder filling).

Motion differs for different parts of the anatomy, and therefore the calculated margin will be different for each part. In the worked example, a larger margin is found for the SV. Many centres would use the same margin, which may cause parts of the SV to be underdosed sometimes. The acceptability of such underdosage is a clinical decision.

Calculation should be consistent with the set-up correction protocol; for example, in the worked example, different margins were found for the prostate and the bone set-up error correction.

Delineation variation should be part of the margin, but measurement of such variation should not include interpretation differences. These should be solved using other means, such as by training or introducing unambiguous protocols.

When correcting for set-up errors (for example, prostate motion), other errors may become dominant. In the example, the registration of bony anatomy on the IGRT system has an accuracy of 0.01 cm, while registration of the prostate is assumed to have an accuracy of 0.2 cm.[28,29]

When margins are very small the definition of the CTV will become more critical, and may have to be revised. For instance, Singh *et al* used a CTV definition for prostate cancer as the dominant lesion, expanded with 4 mm plus the rest of the prostate.[30]

Although some reported studies have analysed images from as few as ten patients, it has been shown that small patient studies of this size can result in a large uncertainty in the population systematic set-up error.[31] The random set-up error estimate is likely to be more accurate even for small patient numbers as long as sufficient images are acquired per patient and interpatient variability is not excessive. The standard error (SE) of the estimate of the SD is given by $\sigma/\sqrt{(2N-2)}$, so to have a 10% SE in $\sum$, a study with 51 patients is needed. With 20 patients, the SE is about 16%.[1] Since $\sum$ dominates in the margin, this SE translates directly into the margin.[1]

Recommendations

- Data used for margin calculation must be relevant to the individual department.
- All errors associated with specific disease sites should be considered and margins should be consistent with the matching and correction protocol.
- Training and competency programmes and peer review of target volume delineation will reduce interpretation error, which is a gross error that should not be included in the margin calculation.
- Observer variation in target volume delineation will remain and must be included in the margin calculation.
- A conservative approach should be applied when reducing margins, as there will be residual uncertainties.

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7. Adaptive radiotherapy

Adaptive radiotherapy (ART) refers to the alteration of the radiotherapy treatment plan to compensate for changes in tumour and/or normal tissue anatomy. It has been defined as 'a closed-loop radiation treatment process where the treatment plan can be modified using a systematic feedback of measurements'.[1]

Anatomical structures including the tumour can change in a number of ways during the course of treatment. Some changes will be slow and systematic and can be caused by physiological factors such as weight loss, disease progression or tumour shrinkage or expansion. Other anatomical changes that occur in the short term can be predicted (for example, bladder filling). However, on a day-to-day basis the amount of filling is typically random. Unpredictable changes also occur (for example, when there is lung collapse or reinflation).

Set-up corrections, which rigidly shift the patient with respect to beams, will not totally compensate for these changes. In other words, the accuracy of the patient geometry model acquired at the time of planning reduces as the treatment progresses.

It is therefore considered good practice to replan the treatment on an updated patient anatomy and geometry when required. This is inherently a multidisciplinary process that requires effective communication between all members and disciplines of the radiotherapy team.

The approaches used to adapt fall into four categories.

- **Reactive ART:** acts on observed changes, typically detected by imaging during the treatment course.
- **Scheduled ART:** schedules replanning in advance for predictable or extremely likely changes.
- **Proactive ART:** predicts changes likely to occur and prepares a choice of plans or 'library' to compensate for these changes. Referred to as the library of plan (LOP) approach.
- **Real-time ART:** creates and delivers a new plan online (on the treatment machine while the patient is in the treatment position). Can occur for each fraction or only when required.

Whether and by how much the patient would benefit from replanning depends on the tumour site and patient-specific characteristics. Considerations for all types of ART are as follows.

1. Anticipated clinical benefit balanced against time and resource implication, as well as patient stability implications

The clinical benefit of any adaptive procedure depends on several factors. Firstly, the geometric impact of changes, such as the amount of motion and deformation of the target and OAR. Secondly, the dosimetric impact of changes in density, which in photon therapy are often extremely small.[2] Such issues are typically evaluated using simulation studies on retrospective data. Centres are advised to develop their own protocols. Circumstances may differ from protocols described in the literature (for example, patient populations, dose and fractionation, treatment delivery methods) and some validation of protocols is always required. A final factor is the short-term anatomical motion that can be expected during the delay incurred by the adaptive procedure. For example, if online replanning for a small

change takes 20 minutes or more then it is likely that the gain of the replan is limited by further anatomical changes, which increase with time.[3,4] Note that apart from dosimetric considerations, changes in patient anatomy may reduce the effectiveness of immobilisation and this can be an independent reason to initiate resimulation and replanning.

2. Thresholds for intervention (quantitative and qualitative)

Thresholds and decision-making tools play an important role in delivering ART. Ad hoc decisions are not recommended and departments are advised to develop protocols to ensure that clinical and physics evaluations are only performed when needed to ensure adequate use of resources. Such protocols will depend on factors such as the tumour site and treatment aim. Currently a number of so-called traffic light decision aid protocols are in use that have been shown to be effective.[5] For example, a decision step could be to evaluate the change in external contour, where only changes over 1 cm will lead to a decision for evaluation and/or adaptation.

3. Implications of previous delivered dose

One of the principal decisions to be made in designing an adaptive workflow is whether to consider the already delivered dose in designing the replan. Caution should be exercised when considering the already delivered dose as assumptions are made regarding the spatial correspondence of tissues from the first plan to the time of the decision to replan. Deviations from the assumptions made can cause the labelling of dose delivered to one region to be erroneously assigned to a different region. In many anatomical sites deformable registration algorithms are considered to be inadequate to provide accurate dose mapping, especially around adjacent OAR that move independently (sliding tissues) and/or OAR that are close to either a regressing or expanding tumour.[6]

Some commercial TPS allow planning with a background dose (they reoptimise the rest of the treatment given the dose distribution delivered so far). This approach would allow dose deficits or surpluses to be corrected. However, if spatial correspondence is inaccurate this could lead to per-fraction hot or cold spots in the patient's anatomy. Extreme caution must therefore be taken if employing this approach. A conservative strategy is to replan each session in isolation without consideration of the previously delivered dose.

7.1 Reactive adaptive radiotherapy

Reactive adaptation refers to making changes to a treatment plan based on observed changes in patient geometry. Such changes are observed through the use of on-treatment imaging modalities such as CBCT. Smaller changes can be monitored to ensure consistency before performing a replan. Some changes may indicate a new medical condition that requires clinician evaluation (for example, large lung tissue changes or a bone fracture). It is imperative that staff are trained to identify such cases.

When using on-treatment scans for the delivered dose assessment, it is important to consider their limitations, such as poor soft-tissue contrast, field-of-view restrictions and image artefacts. The accuracy of dose calculations based on on-treatment scans should be validated locally.

The most commonly used on-treatment modality is CBCT, with MRI now starting to be used.[7] Neither modality provides calibrated Hounsfield units. Methods to make such scans suitable for dose calculation are bulk-density override assignment or deformable registration of the planning CT. For CBCT, scanner and site-specific Hounsfield unit-to-

density lookup tables could be generated.[8] Shading correction algorithms have been proposed, as well as machine-learning-based approaches.[9–12]

An accurate update of target structures and OAR is essential to perform a full dose-volume histogram (DVH) analysis. Automated tools in the TPS can streamline this process (for example, automated segmentation or contour propagation using deformable image registration (DIR)). Such algorithms require careful commissioning and validation, and contours generated by automated segmentation should be checked visually and adjusted if necessary.[13] It should be noted that tumour regression generally does not imply shrinkage of the CTV.[14] Therefore, reduction of the CTV should be avoided outside clinical trial settings to establish potential safety. For instance, if the CTV is defined by a margin, a rigid transfer of the original CTV from the planning CT to the replan is recommended, which should only be adjusted around anatomical boundaries.

Using the Hounsfield-corrected on-treatment scan and the original beam set-up and monitor units a new dose distribution is next calculated and then evaluated by means of DVHs of the updated structures. The DVH parameters that are used to trigger adaptation are not necessarily the same as the ones used for plan optimisation. In particular, PTVs and organ PRVs are designed to absorb some anatomical variation, thus some loss of PTV coverage or increase of PRV dose should be considered.

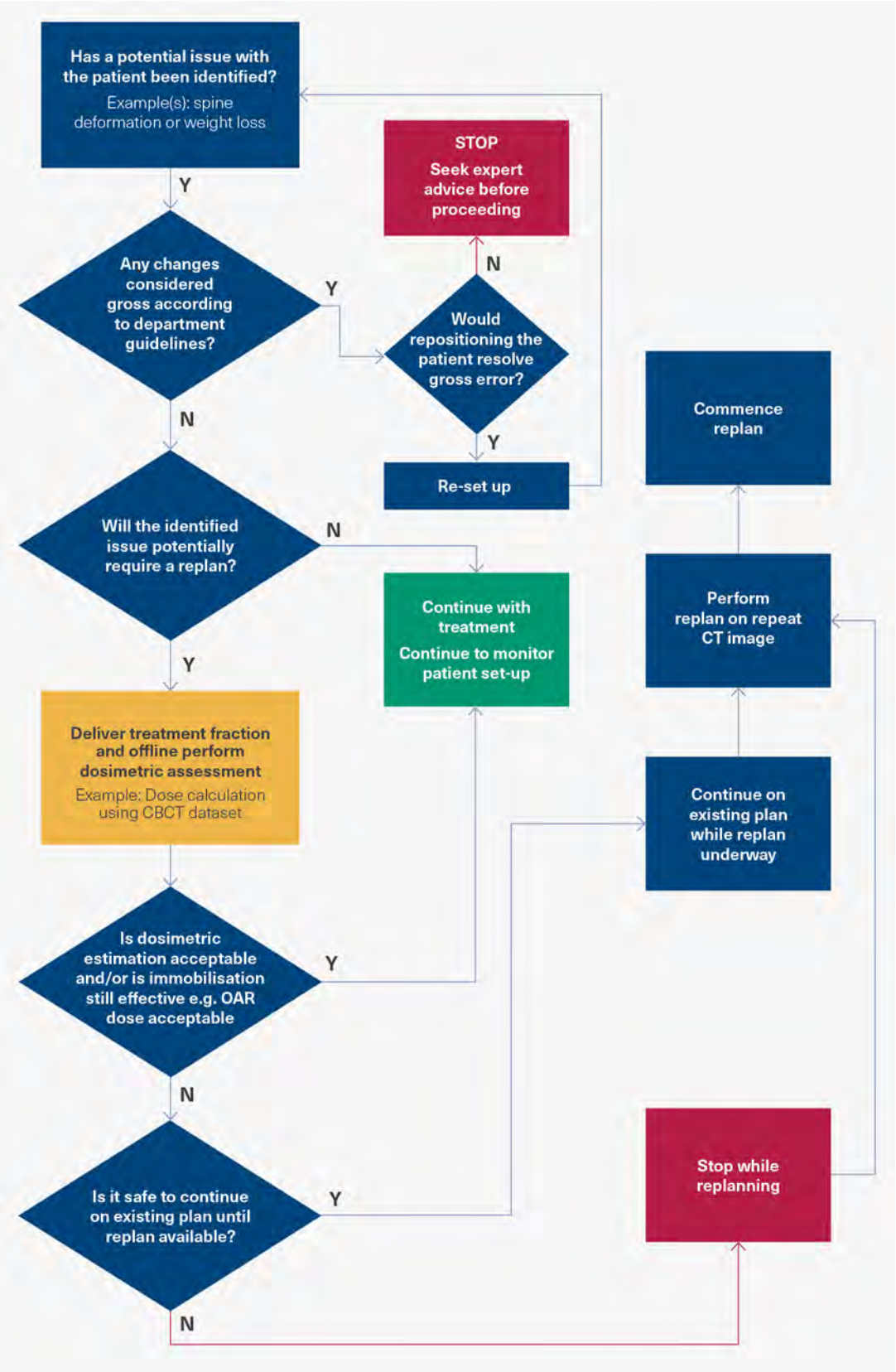
Many centres would acquire a repeat planning CT if the evaluation showed a replan to be necessary. In some cases it may be possible to replan using the original CT, the CBCT or a combination thereof.

One of the biggest challenges of reactive adaptive planning (replanning) is the ability to generate a new treatment plan in a timely manner. This requires appropriate staff groups to be available when needed and workflows to be clearly defined. Despite the accelerated timeframe required for a replan to be generated, appropriate planning and checking processes must be maintained to ensure the safety of the radiotherapy treatment.

The results of a dosimetric estimation should be reported to the MDT to determine whether a replan is clinically justified. Once sufficient experience has been gained locally, the decision to replan could be performed by an entitled registered healthcare professional such as an appropriately trained senior radiographer or MPE.

An example of a recommended workflow, using weight loss for a head and neck patient as an example, is given in Figure 9.

Figure 9. Typical workflow for reactive adaptive planning, using weight loss for a head and neck patient as an example



When performing a replan, processes should be clearly defined in local procedures for adaptive replanning to ensure that the correct plan is delivered from the date intended and the correct fractionation is scheduled in the R and V system.

Recommendations

- **When:** the reactive replanning process is initiated when anatomical changes are observed through imaging during the treatment course that are deemed to cause a significant change in the delivered dose to the relevant anatomy compared with the original planned distribution.
- **Time:** unscheduled reactive replanning can be performed at any stage during the course of treatment. Smaller changes can be monitored to ensure consistency before performing a replan. Replanning during the final few fractions may be impractical due to the time required to generate a new plan.
- **Training and competency:** specialist training is recommended for identified staff on adaptive replanning, including site-specific imaging training for radiographers to identify changes that may affect delivered dose or that indicate a new medical condition. Tumour site-specific protocols should include a system for evaluating when action is necessary based on local experience and balancing the resource requirements for replanning with the benefit for the patient's treatment outcome.[15] Local rules should define the individuals entitled to request a replan.
- **Resources required:** staff, equipment and software for dose evaluation need to be clearly defined, along with rapid access to planning CT where indicated.
- **Safety:** although some planning systems have tools available to incorporate previously delivered dose into a treatment plan, the use of these tools is not currently recommended.

7.2 Scheduled adaptive radiotherapy

For specific tumour site groups replanning the treatment can be performed at one or more predefined time point(s). This is the case for tumour sites that have predictable changes in anatomy and therefore benefit from scheduled replanning, such as patients with head and neck cancer who show consistent weight loss, shrinkage of tumour and/or change in the OAR (for example, parotids).[16]

Scheduled replanning allows for the advance scheduling of extra patient imaging appointments that may be required and can lead to a more predictable workload for the department. It can be considered as a natural progression from conventional non-adaptive planning with multiple phases.

A disadvantage of scheduled replanning is that sometimes unnecessary replanning is performed.

Recommendations

- **When:** for patient groups that consistently show a change in anatomy.
- **Time:** before the middle of treatment in the majority of scenarios.
- **Training and competency:** minimal extra requirements.
- **Resources:** extra CT scan and planning sessions (but known beforehand).
- **Safety:** new plan must be adequately quality assured; although some planning systems have tools available to incorporate previously delivered dose into a treatment plan, the use of these tools is not currently recommended.

7.3 Proactive adaptive radiotherapy – library of plan approach

The proactive ART process predicts changes that are likely to occur and prepares a choice of plans or 'library' to compensate for these changes. This approach may also be referred to as 'plan of the day'. It will be refered to in this document as the library of plans (LOP) approach to avoid confusion with online ART. Following online image review, this solution accesses a library of plans from which a single plan with the best-fitting dose distribution for the anatomy seen at that fraction is selected for treatment, with or without table shift. This strategy has been applied to tumour types subject to large interfraction variation and which exhibit an element of predictable geometric change, typically as a result of organs filling or emptying.[17–19]

Many groups have demonstrated proof of principle and dosimetric advantage of LOP over a single plan created from the planning CT scan. They illustrate that improved target coverage and normal tissue sparing can be achieved.[19–21] Planning studies reflect a further step-wise reduction in integral dose to surrounding normal tissue will be achieved with online replanning at these sites.[22,23] Until an online replanning strategy is widely accessible, LOP bridges the gap between clinical need and an adaptive solution.

Plan selection on set requires additional fraction time. For example, in bladder LOP this has been reported to be an additional five minutes but could be up to 20 minutes per fraction.[20,24,25] Appropriate plan selection at treatment is based on achieving optimal target coverage with minimal normal tissue irradiation. In some circumstances, none of the plans in the library may appear to achieve this. In this situation it may be appropriate to consider removing the patient from the couch and implementing an intervention that may assist with the patient 'fitting' into the existing library prior to reimaging. Intervention will depend on anatomical site (for example, in pelvic treatments voiding or drinking). For conventionally fractionated treatment courses it may be pragmatic to consider target prioritisation over OAR considerations if no plan appears favourable. Repeated use of this approach or if adopted for hypofractionated courses may result in significant deviation from initial planned constraints and so should be used with caution.

7.3.1 Deriving the library of plans

A number of methods have been reported as useful for creating the LOP. However, there is no accepted consensus as to the best method of generating this library. The methods can be broadly divided into three techniques.

1. Library created from a single planning scan

A series of plans is created using PTVs of varying sizes. The different PTVs are generated by applying varying margins, possibly anisotropic, around the CTV derived from knowledge of expected changes seen within the index population.[26,27] The benefit of this library creation approach is that it requires a single planning CT, can be used from the first fraction and can be generated with standard margin tools.

2. Library created from multiple planning scans

An attempt is made to reproduce potential individual interfraction variation by acquiring successive planning scans for that patient. This approach can also be implemented from the first fraction.[28,29] For example, it is known that cervix-uterine motion is predominantly controlled by the filling status of the bladder.[19] Therefore two planning scans – one with an empty bladder and one with a full bladder – are acquired. A method of interpolation of position is required to create the intermediate plans.[19,29] Unfortunately, currently none of the planning systems provides such methods and in-house solutions have therefore been used.

3. Library created from planning scan and volumetric images acquired on treatment

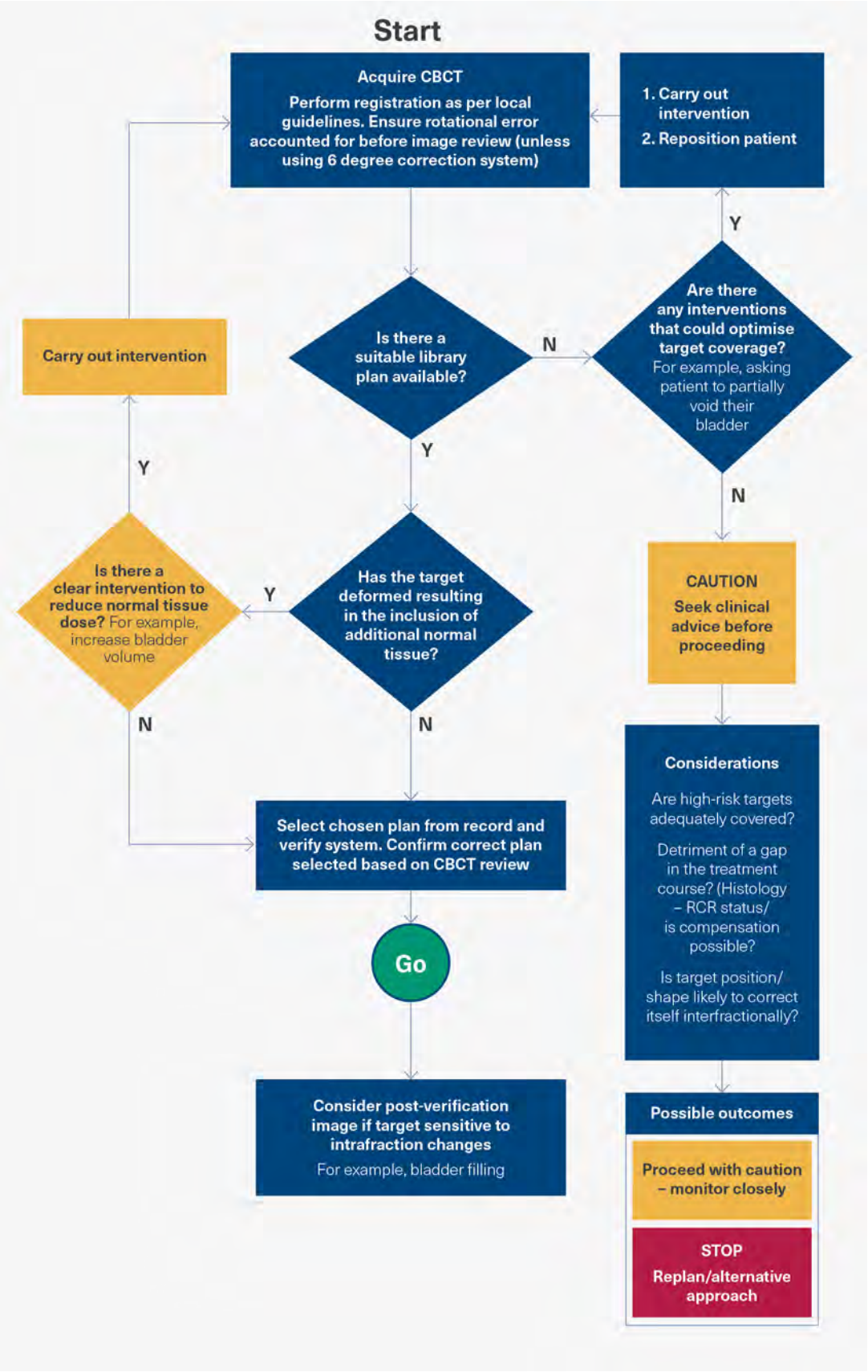
This approach uses repeat volumetric imaging to evaluate the range of interfraction changes.[24,30] Typically five scans are acquired in the first week of treatment.[30] This means this method cannot be used for all fractions from the start of treatment and is not applicable to hypofractionated treatments.[31] Another approach, which would be applicable to hypofractionated treatments, is to acquire planning CTs on several days prior to treatment.[32]

The library of plans can, for example, be created as follows. Three PTVs are created: smallest, largest and medium, all including some extra margin above the applied CTV(s). The smallest PTV is created from the smallest CTVs (CTVsmall) seen on either the planning CT or repeat scans; the largest PTV is created from the composite of all CTVs using a Boolean 'or' operation (CTV_{large}); the medium PTV is created from a selected CTV whose volume and shape lies between CTV_{small} and CTV_{large}.

The number of plans created for use in the library has resource implications in terms of planning time, QA and decision-making time for online plan selection. Automated planning can help reduce planning workload to some extent.[33]

A library that is not well designed can lead to a number of issues. Too many plans may also increase the likelihood of error, such as selecting one plan for treatment but delivering with another because the R andV systems do not fully support LOP approaches.[34,35] Too few plans to cover the spectrum of expected interfraction change will result in poor conformality.[25] A proposed summary workflow outlining the LOP adaptive approach is shown in Figure 10.

Figure 10. Summary workflow for library of plans adaptation strategy



Plan selection should allow sufficient coverage to accommodate intrafraction motion. Therefore, on implementation, post-treatment volumetric imaging is recommended to confirm this.[27,25]

When performing LOP, processes should be clearly defined to ensure that the correct plan is delivered and documented in the R and V system.

Radiographers should receive specialist training and competency assessment within a structured learning and training programme that includes anatomy of relevance and protocol-specific decision-making guidelines.[36,37] Radiographer competency can be successfully maintained by ensuring that a minimum number of plan selections are reviewed (on or offline) regularly within a portfolio of professional development.[37] Regular audit of concordance between online radiographer plan selection and offline clinician plan selection is recommended.[37]

Recommendations

- **When:** for tumour sites with large expected CTV variation, typically due to bladder or rectum filling.
- **Time:** prior to treatment or after the first week for an approach based on CBCT images.
- **Training and competency:** radiographers should receive specialist training and competency assessment.
- **Resource:** additional time required for plan creation and selection should be factored in.
- **Safety:** plan selection should allow for intrafraction motion. When LOP processes are not supported by R andV systems, careful manual procedures should be defined to avoid incorrect dose delivery.

7.4 Real-time adaptive radiotherapy

Real-time ART creates and delivers a new plan online (on the treatment machine while the patient is in the treatment position). It can occur for each fraction or only when required.[1]

The benefits of real-time ART include the ability to correct for changes that cannot be accounted for by simple couch shifts (for example, change in tumour size) or that are too rapid for other adaptive approaches (for example, variable distance between pancreas and duodenum). Real-time adaptive planning still does not account for intrafraction changes, so sufficient intrafraction stability is currently a requirement for this approach.

Although real-time ART has been closely tied to the introduction of MRI-guided radiotherapy, it is also possible using other technologies such as CBCT.[38–41]

Several groups have had early experiences using these new technologies, reporting dosimetric benefits in tumour sites such as pancreas, lung, adrenal and other tumours.[42–46]

The tools (hardware and software) required to facilitate this process are still in the early stages of implementation and this is a rapidly evolving field with a need for improved speed, workflow, accuracy and robustness. Post-treatment imaging is important to review decisions and safety.

Key requirements for the integration of real-time ART into the clinical process are sufficient image quality for accurate registration and manual/automatic segmentation and efficiency of the process to allow completion of the workflow in an acceptable time for the patient and department.

Other considerations include the ability to evaluate each fraction in isolation to guarantee the delivery over the treatment course is safe. It has also been suggested that the capability to choose a base plan from all previously treated plans for a given patient in a given course is beneficial.[47]

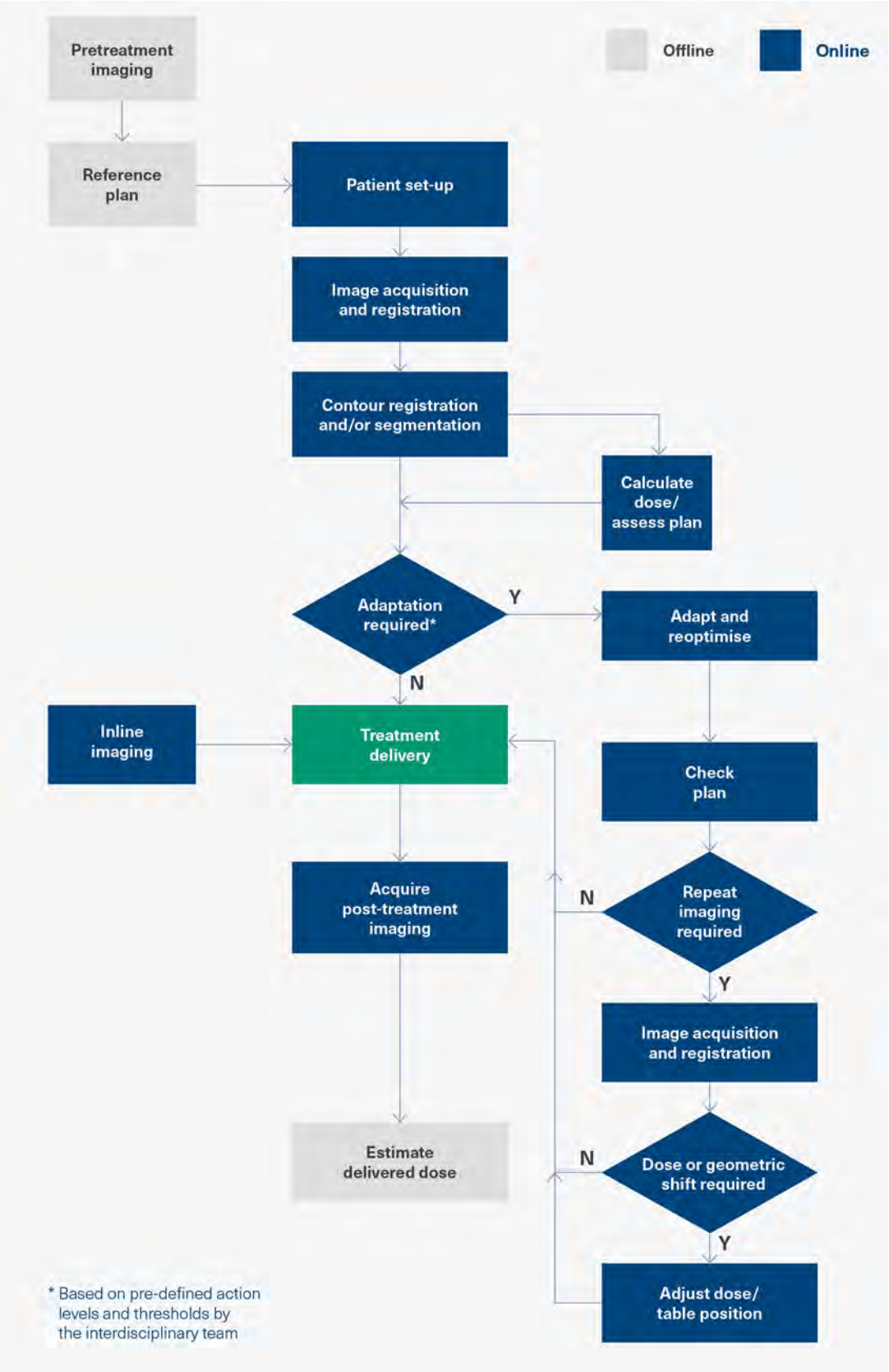
In addition to the considerations above, key to implementing real-time ART into the clinic is a clear pathway with the appropriate tools and resources, including appropriately educated and experienced team members. Real-time ART is currently staff resource intensive, with all members of the IGRT MDT required to be present at the time of treatment. To improve efficiency and clinical implementation, traditional roles and responsibilities will need to change and evolve.

Offline review of the real-time ART practice is required to evaluate the impact on the clinical service. When online ART leads to changes in margin or dose prescription, acute/late toxicities and survival outcomes must be carefully monitored to ensure absence of unexpected outcomes. For instance, more local failures were reported after improving accuracy of image guidance and shrinking margins, which may be due to miss of subclinical disease.[48] Local evidence is required to ensure a robust practice, such as evidencing practice through offline planning studies, end-to-end process testing and inter-observer agreement studies.

As we come closer to realising real-time ART strategies based on geometric changes (for example, tumour size, shape or position), the potential for real-time biologically adapted radiotherapy also becomes more tangible (in specifically designed clinical trials). However, regardless of the strategy, the development of a safe, effective workflow with sufficient QA that has been validated locally is paramount to the successful implementation of real-time ART.[49]

Groups reporting on their early experiences with real-time ART typically use a similar workflow with slight variations.[50,51] Below are our recommendations based on these published reports (Figure 11). With online ART, all tools are integrated into the treatment machine. However, sufficient additional workstations with these capabilities are required to prepare the cases and perform offline evaluations.

Figure 11. Proposed real-time adaptive workflow diagram



Recommendations

- **When:** when there are gross unpredictable interfraction changes with limited intrafraction motion; hypofractionated treatments; where there are highly critical mobile OAR.
- **Resources required:** availability of multidisciplinary team for implementation; identification of threshold and action levels; additional time on treatment machine;[52] sufficient workstations for offline preparation and evaluation.
- **Training and competency:** extensive training is required for all staff roles such as MR safety (if applicable), patient set-up, imaging, delineation, planning, QA, delivery and monitoring. In contrast to most other forms of radiotherapy, all disciplines are represented at the treatment unit. Therefore communication and decision protocols are crucial.
- **Safety:** needs to be delivered in a safe environment with suitable (and frequent) audits of accumulated dose and online/offline QA processes. Back-up procedures must be in place. All processes performed should be undertaken by registered healthcare professionals with clearly defined roles and responsibilities.

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8. Evaluation and change of IGRT practice

8.1 Introduction

As radiotherapy is in a state of rapid evolution there will always be the need for institutions to change and improve their IGRT practice. Each department should have an ethos of ongoing, continual improvement that is evidence based and underpinned by risk-based thinking. Implementing change can be challenging, particularly in a busy, high-throughput clinical environment.

Change is a managed process, with management structures designed to promote continuous process evaluation and facilitate potential improvements. Risk assessment for change is essential. Clear documentation of the proposed change is required, which starts with the need to understand the current baseline, understand the change and then measure the impact of the change.

This section sets out a framework for evaluation and change. It describes the various roles and responsibilities, considers how opportunities or drivers for change might be identified, then discusses the change implementation process itself.

8.2 Summary of the change management framework

The change management process can be encapsulated by critically working through the following questions.

- What are our motivations?
- Should we be doing this and what are the risks and the benefits?
- Are there safety implications?
- Are the right people involved and how do we know?
- Do we have the knowledge and expertise to implement this successfully? Are there training implications?
- Has the change been planned and can we stop or undo the change if required?
- How will we know whether we have achieved what we set out to do and whether the change has made things better?
- Is communication organised appropriately?

8.3 Multiprofessional roles and responsibilities

Therapeutic radiographers as the end users are well placed to implement improvements, although the need for change can be identified by any member of the MDT.

Leads for IGRT change should be identified and multiprofessional meetings held on a regular basis with multidisciplinary input when required. These meetings should include a general review of current processes and feedback on ongoing development work. The change leads should be resourced and empowered to fulfil their duties effectively. Table 11 shows the multitude of roles and responsibilities in the IGRT process and these should be considered in the change process. Many of the roles can be performed by appropriately trained individuals from each of the disciplines involved, such as clinicians (doctors), dosimetrists, clinical scientists specialising in radiotherapy physics, medical physics experts and therapeutic radiographers.

Table 11. Indication of IGRT roles that need to be performed by the MDTs involved in the IGRT process

Roles and responsibilities
Act as IR(ME)R practitioner, providing justification for exposures
Provide clinical input and decision-making during treatment planning in complex or non-standard cases
Ensure imaging processes are consistent with the overall clinical vision, linked to clinical protocols
Guide the interpretation of verification images, particularly for new techniques or challenging cases
Project manage and develop IGRT
Take day-to-day responsibility for acquiring, actioning and approving verification images/data
Develop IGRT protocols
Develop and manage IGRT training package
Analyse set-up errors to inform margin calculations
Accept and commission IGRT equipment
Raise awareness of IGRT equipment capabilities and stimulate interest in their implementation
Develop and maintain QA programmes for IGRT
Optimise IGRT protocols/doses, including measuring the radiation doses for imaging protocols and maintaining registers of patient imaging doses
Consider how CTV to PTV margin expansion is linked to available IGRT protocols
Provide advice on how image matching should be prioritised for difficult cases based on an understanding of the treatment plan
Perform patient dose assessments using IGRT data sets (eg, when a patient has lost weight during treatment)
Apply adaptive processes using IGRT data sets

8.4 Identifying the need for change

Departmental IGRT processes should be reviewed regularly alongside overarching clinical protocols. A formal review should occur at least every one to two years, although reviews can also be triggered by emerging evidence, the availability of new treatment equipment or a revision to a treatment technique.

This evidence may take many forms including:

- Peer-reviewed literature
- Presentations at conferences
- Locally collected evidence, including clinical audits

- Sharing of experiences between centres
- Information from a manufacturer (for example, release of new feature or changes to workflow)
- Learning from incidents; departments should have a record of errors and near-misses and, where incidents are deemed reportable, these should be referred to the appropriate national regulator.[1]

Ongoing audit of processes is a requirement for accredited quality management systems and is also an obligation under IR(ME)R. The British Standards Institution quality management standard (BS EN ISO9001:2015) concisely describes the requirements for an internal audit programme.[2] The National Institute for Health and Care Excellence (NICE) has provided guidance that can also be referred to when setting up audit programmes.[3]

Intradepartmental cross-disciplinary audit is recommended to assess protocol compliance within a particular staff group and has the advantage of familiarising staff groups with each other's practice.

Additionally, it is prudent to seek advice from other departments or professionals when specific questions arise. Suggestions for useful contacts and sources of expertise are:

- Manufacturer user group meetings
- Professional user group meetings
- Study days
- Professional bodies
- Mailing lists (for example, radiographer imaging list, medical physics lists)
- Radiotherapy networks.

A review of both the quantity and category of IGRT queries that are being dealt with can prove beneficial for identifying the areas on which to focus attention within a department.

Given the time pressures in many departments and also issues surrounding patient discomfort, consideration should also be given to ensuring the efficiency of the IGRT processes.

In addition, the radiotherapy operational delivery networks (ODNs) in England could provide a forum for various centres to agree IGRT protocols across the centres in the ODN.

8.5 Implementing the change

A well-managed project should include a number of stages, each involving multiple steps. Each stage is iterative in nature and any learning points identified may require a change or moving back to an earlier stage.

It is also important to note that the preparation or planning phase of the project represents the majority of steps. Planning and critical thinking before acting are crucial to a successful project.

Application of the change management framework is illustrated in Appendix 14.2 by working through the implementation of online 4D cone-beam CT (CBCT), which is now readily available.

Project stage 1: define the goals

Any project starts with a clear statement of overall goal, including a justification for why the change is necessary.

Note that the implementation or refinement of certain IGRT processes may enable subsequent changes in other radiotherapy processes. For example, daily volumetric imaging with online set-up corrections may facilitate the reduction of CTV-PTV margins and then dose escalation.

Identification of project leads

A single individual should be responsible for leading the project. This individual is responsible for ensuring the necessary steps are carried out and the MDT described below remains engaged and focused during the project.

It is strongly encouraged that each IGRT project has an identified representative from each of the professional staff groups: radiographers, oncologists, physicists. This representative is responsible for communicating among their teams.

Project stage 2: establish the baseline

Description of the current state

Describe the current status (for example, using an existing audit).

Identification of factors that will inhibit the change

Factors that may inhibit the change should be identified (for example, lack of staff availability, availability of a software licence or training burden).

A tool such as a fishbone or Ishikawa diagram may aid in ensuring all relevant factors are considered.[4,5]

Project stage 3: design and prepare

Risk assessment

Generally, the effort associated with managing a project should be commensurate with the risk and severity of something going wrong.

IR(ME)R requires that special consideration be given to the risk of accidental or unintended exposures. In the context of imaging this applies both to the imaging exposures themselves and the impact on the delivery of the therapeutic dose as a result of the decision-making based on the imaging.

Mitigation of risks

Unacceptable risks should systematically be worked through to ensure that mitigation is sufficiently addressed for each one.

Preparation of list of actions, with owners and timelines identified

Includes preparation of initial procedures and work instructions and development of appropriate training packages.

Regular review of actions

Use as a means to build learning and develop documentation.

Project stage 4: test and refine prior to full implementation

End-to-end test

End-to-end testing of any new process should take place before any change is implemented.

End-to-end tests should cover all the steps in the process, in real time and in clinical mode.

Pilot project

Pilot projects are a way to demonstrate technology and processes in action. If the change is significant, a pilot project can measure and monitor the initial impact and provide evidence to allow more widespread implementation.

Pilot projects can include implementing change on:

- One tumour site/treatment indication
- One treatment machine
- An agreed number of patients.

Review of pilot and preparation of final project documentation

Data collection should form part of any pilot study undertaken to measure the change that will help determine the effectiveness and/or impact of the change. This can take a variety of forms such as assessing patient/staff experience, resources required, capacity, extra dose and ultimately, the benefits and risks of the change to the patient.

When assessing impact, it is important to recognise what may be short-term and longer-term requirements. For example, unfamiliarity and training can have an impact on time; however, this may only be an impact during initial implementation. A more significant change may require a longer treatment appointment and so capacity may need to be investigated.

Technical, clinical and dosimetry data and information should be used to measure the effectiveness of the change as well as opinions from both patient and staff experience, if appropriate.

Once the pilot data have been compiled, they should be fed back to the MDT for consideration of implementation of the change into the routine service.

Project stage 5: full implementation and review

Project go-live

Before clinical implementation can take place there must be communication with the wider team to ensure awareness of the change.

For those for whom the change will have a direct impact, information, question-and-answer and training sessions are vital to ensure everyone is engaged in and confident with the change prior to implementation.

Documentation and protocols should be updated and in place, and in the case of significant change, with practical reference summaries available.

Continuous monitoring needs to take place to ensure the initiative is progressing as expected from the pilot. Any unforeseen challenges should be assessed and addressed in a timely way by the MDT.

Learning from feedback: lessons learned sessions

The journey of change should be documented, including analysis of the full clinical implementation, such as what went well and what to do differently next time.

Learning from the experience and change management process is valuable to allow for smooth and efficient future implementations.

Sharing the change experience with both the local team and beyond is a valuable part of the process. Where appropriate, dissemination and sharing of the results of the change is encouraged so that other centres can build on and learn from the local experience.

8.6 Training

8.6.1 Training in the change management process

Change management training is available from a range of sources. NHS Improvement has provided a useful overview of the change management process and systems and tools available for managing change.[6] The majority of hospitals provide their own project management training and the professional bodies also offer a range of relevant management courses.

8.6.2 Training in the processes that have changed

Within any change management process it is imperative that alterations to procedures are communicated to all relevant personnel and, if required, that updated training and a review of competencies is carried out in a timely manner (see Section 9).

8.7 Conclusion

Regular, iterative change should be welcomed and embraced. When managed well, the risk from change is minimised and implementation is achieved smoothly and safely, without unnecessary anxiety. A concise project plan with actions can be used to guide and document this process. An example is shown in Appendix 14.3.

It is often better and more natural to advance via small steps frequently than to attempt to undertake large steps forward at extended intervals. It also empowers individuals to recognise that making changes is within their power and promotes a more in-depth understanding of the clinical application of available technology.

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9. Training and competency

9.1 Introduction

As IGRT is a core component of modern radiotherapy, robust training programmes are essential. Training of personnel and maintenance of IGRT competencies are integral to the implementation and daily utilisation of IGRT, ensuring patient safety. Comprehensive training programmes ensure standardised protocols are implemented for all staff and that each individual is skilled to a consistent level. This can reduce interobserver variability, improve safety and increase efficiency. Departments should be enrolling newly qualified members of staff into their training programme so that optimal protocols can be rolled out to more patients.

The modality of IGRT required varies depending on the anatomical site, motion of soft-tissue structures and delivery techniques. Departments must consider the training implications of each IGRT technique and develop training and competency assessment accordingly. A local register of incidents is also a valuable resource to evaluate training needs.

9.2 The core components of IGRT training for all staff groups

- IGRT implementation process and quality documentation
- Understanding of acquisition modes
- Knowledge of optimisation of imaging protocols, hardware and software
- Knowledge of image registration and analysis of set-up error
- Knowledge of decision-making and problem-solving
- Assessment for treatment suitability and plan modifications
- Justification of exposure and understanding of scope of practice
- Knowledge of site-specific anatomy and motion, as well as commonly expected medical issues
- System-specific application training based on discipline
- Understanding of IR(ME)R legislation.

9.2.1 Discipline-specific training

Each discipline will require specific IGRT training to best fit its responsibilities. Responsibilities vary between departments and are dependent on staffing models and changes in the workforce. Training will overlap between disciplines as roles and responsibilities expand. Where new technology is implemented, MDTs should optimise its use to best fit workflows and patient pathways. Training must also adapt and evolve alongside changes in practice, equipment, service requirements and experience.

An understanding of IR(ME)R legislation is required by all. Local training for new duty holders within this framework should be provided to inform them of local justification, authorisation and optimisation working practices. Individuals must be confident of their responsibilities and of working within their role as operator, practitioner or referrer.

9.2.2 Multiprofessional IGRT specialist group

It is recommended that every department has an overarching IGRT specialist team responsible for ensuring appropriate application of IGRT across the service. Consultation between multidisciplinary specialists (radiographers, physicists, clinical oncologists and

dosimetrists) is essential when developing treatment site specific IGRT protocols, to ensure expert representation. Sharing of information from established sites in conjunction with site visits should enhance any development work by strengthening understanding of the clinical application. Where appropriate, inclusion of diagnostic colleagues should be considered to harness their experience, tailoring and optimising image quality for specific applications. To facilitate this, it may be necessary to orientate supporting diagnostic colleagues in radiotherapy.

9.2.3 IGRT specialist

It is recommended that every department has one or more IGRT specialists to support clinical implementation and application of IGRT. In each department there should be at least one radiographer and one MPE IGRT specialist. An IGRT specialist should:

- Have undertaken a recognised national or international IGRT training programme (for example, the European Society for Radiotherapy and Oncology (ESTRO) IGRT course) or have successfully completed an MSc module in IGRT
- Have completed QA internal/external accreditation for related trials
- Have undertaken manufacturer applications training
- Have in-depth knowledge of the type of geometric errors that can occur in radiotherapy practice and methods to minimise these
- Keep abreast of emerging IGRT technology and research to inform best practice
- Regularly interact with other IGRT specialists, outside of their service, to ensure a wide scope of knowledge is maintained
- Participate in peer review of IGRT practices
- Be clinically competent in the regular delivery of IGRT and authorised to sign off other radiographers and if appropriate other disciplines as competent
- Be effective educators, competent to cascade their IGRT knowledge
- Lead in the service development of new IGRT technologies and their applications
- Be a source of advice where complex cases arise
- Ensure MDT involvement from all disciplines
- Maintain a record of training delivered to staff groups
- Have a clear understanding of IGRT benefits versus radiation detriment in relation to justification of concomitant imaging dose.

9.3 Training requirements

9.3.1 Training content

Training programmes and requirements will depend on equipment used and clinical protocols (see Table 12). Roles – and therefore training requirements – will vary between departments. For all disciplines it is worthwhile to be familiar with all aspects of IGRT, but in practice that may not always be achievable. Multidisciplinary meetings are encouraged to share best practice and facilitate training.

Table 12. Suggested components of IGRT training

IR(ME)R responsibilities
Departmental imaging protocols
Image quality optimisation
Imaging dose justification
Image transfer to/from TPS
Reference image production
Image acquisition methods/modalities
Image registration
Image analysis methods including automatic/manual matching
Image interpretation and decision-making
Review of target and OAR coverage
Understanding of tolerance levels and action levels/triggers (eg, decision-support traffic light system)
Knowledge of systematic and random errors
Relevant clinical trials
Quality assurance (QA)

In addition to generic specialist training the following issues should be included in **treatment site-specific training**:

- Staging and management options
- Relevant anatomy
- Anatomy motion studies
- Image interpretation experience
- Worked clinical examples
- Assessment of target volume coverage
- Review of OAR volumes
- Disease-related events (for example, collapsed lung or pneumothorax) affecting treatment suitability
- Factors influencing decision to not treat or rescan (bladder/rectal volume).

For new and more complex techniques additional advanced training should be provided in, for example:

- LOP selection
- MRI-guided treatment
- Plan adaptation
- SABR
- Off protocol/out-of-tolerance decisions
- Implementation of new techniques/working under concession.

9.4 Training methods

Training may be internally or externally accredited. The content of internal training programmes should be devised or advised by the multidisciplinary IGRT specialist team. Thought must be given to the appropriateness of training duration, availability of training, pre-existing knowledge and individuals' learning styles.

When introducing new training, feasibility and suitability should be assessed initially within pilot work. There should be a limit on the number of trainees recruited or the number of treatment sites covered within the pilot. Pilot result analysis should be used to inform and update training before disseminating further.

9.4.1 Training formats to consider

Training programmes are often composed using a multi-method format:

- Manufacturer training
- Training workbooks
- Multimedia presentations
- One-to-one training
- Training lectures, multidisciplinary delivery
- Observational training, including external site visits
- Peer-reviewed test cases
- E-learning
- Evidence-based training
- Group continuing professional development (CPD) sessions, with multidisciplinary input
- Trial accredited training
- Visit to 'lead' department
- Professional body training/accreditation.

9.5 Competency assessment

When formally assessed on a regular basis, departments can ensure standardised delivery of IGRT that allows reduction of variability and documentation of current standards and provides a starting point for training new operators and a baseline from where improvements can be made to the service. It ensures that professional development is recorded and acknowledged for all disciplines, as per responsibilities.

9.5.1 Competency assessment methods to consider

The following methods may be considered to assess competency:

- Assessment of baseline skills
- Self-assessment
- Reflection
- Test
- Imaging database – gold standard comparison (ensuring a wide range of clinical cases/ situations)

- Delineation of target anatomy – for clinical oncologists this may take the form of trial test contouring cases
- Online assessment
- Timed review
- Pre- and post-training assessment
- Ongoing peer review.

Training databases are recommended for education and assessment of an individual's competency. Training cases should be selected from previous patients demonstrating a wide variety of clinical scenarios and IGRT challenges. The baseline gold-standard assessment should be undertaken by the individual or team identified as an 'expert' in that task. Ideally, the review process during training, including the software used, should mimic the clinical method where possible.

Clear guidance on the assessment process is imperative to ensure standardisation of results between expert and trainee observers. The level of acceptable concordance (pass mark) required must be predefined. Specialist team consensus, supporting literature, statistical considerations and department requirements should guide this.

9.5.2 Maintaining competency

Maintaining competency ensures the ongoing quality of an IGRT service. The degree and frequency of follow-up competency assessment or review required depends on the complexity of the IGRT technique implemented, patient numbers and experience with the technique. For example, when a technique is frequently used, offline imaging audits could be used to assess ongoing competency, whereas for rarely used techniques (low patient numbers) a minimum number of cases should be completed online or offline regularly (for example, each year) to maintain the advanced competencies and ensure standards are maintained. Change in practice or technique developments should be disseminated appropriately across staff groups, with competency updates to reflect this. All staff should take positive ownership of maintaining their knowledge of evidence-based practice.

Methods for assessing continued competency include:

- Self-reflection
- Case reviews
- Audit of online practice
- Portfolio of relevant experience
- Second imaging database
- Peer review.

An example of an IGRT training and competency programme is shown in Appendix 14.4.

10. Site-specific guidance

10.1 General considerations

This section details site-specific recommendations for imaging protocols, starting with the most common clinical sites and ending with palliative radiotherapy. Most principles that apply to all sites are described in the preceding sections. It must be noted that because this is a rapidly evolving area under intense investigation at present, protocols should be reviewed regularly with the most recent evidence obtained in the literature. Note that the preceding sections focus on daily online image guidance, while many of the site-specific protocols still include offline image guidance protocols, which so far have the largest evidence base. Daily online IGRT can often be justified depending on clinical requirements and taking the additional time spent on the treatment unit into consideration.

For all protocols, a CT slice thickness and spacing of 3 mm or less is recommended. Such spacing limits uncertainty in the definition of the longitudinal boundaries of the organs and target. If needed, finer spacing may be selected upfront for the acquisition, and often CT scans can be reconstructed with a finer spacing from the same acquisition data.

In some tumour sites that require large field lengths it may not be possible to include the whole treatment volume in one image. Alternatives include using two CBCTs and some systems allow merging of images, using kV imaging in addition or prioritising the high-dose area or where OAR are at most risk.

There are some aspects of image guidance that are relevant to all tumour sites as follows.

10.1.1 Patient non-compliance

If multiple repeat scans are required, or large set-up errors are identified at the post-treatment registration, there may be an issue with patient compliance or unsuitability of immobilisation. This will require MDT discussion prior to the next fraction. Options could include:

- Modifications to immobilisation or improvement of comfort through use of sedatives or analgesia
- Discussion of the patient's suitability for SABR or consideration of replanning as a conformal treatment.

10.1.2 Vacuum bag failure

An initial attempt should be made to reposition the patient using a new bag, reproducing the previous position as accurately as possible using all available information (set-up instructions, photographs etc) with the aid of the MDT. MDT discussion is essential and, if the subsequent set-up is not considered acceptable following the rescan, a replan in the new position will be required.

10.1.3 Difficulty in mask fitting

In many tumour sites anatomical changes during the treatment may result in difficulty in mask fitting. In some cases, where the mask becomes too tight to fit, it may be possible to cut some regions of the mask out, but it should be confirmed that the stability of the mask remains. Where there are marked anatomical changes during a course of treatment, it may be necessary to make a new mask, rescan and recalculate the plan to ensure adequate coverage and that OAR doses remain in tolerance.

10.1.4 Image registration

Robust image registration depends on critical assessment of the image and appropriate use of the tools available. A volume of ROI is a useful tool to select the most relevant anatomy for registration and as a guide for its validation. It is important not to include anatomy that could adversely affect the registration, such as the femur in patients with prostate cancer where rotation of the femurs could dominate the registration and not result in a true representation of the pelvic position, or the mandible in patients with oral cancer, which may not be stable.

It is good practice to examine the reference image prior to registration to identify the expected position of the target and OAR. In addition, it is important to identify potential mobile objects inside the ROI that may adversely affect the registration procedure. For example, vessel calcifications close to the prostate can be mistaken for fiducial markers. Similarly, contrast in the big vessels may be detected as bone in the registration algorithm. Adjusting the image window and contrast levels is important to ensure best visualisation of the target and OAR and should have a similar appearance to the reference image.

Deformation of the target and OAR can adversely affect the registration and care must be taken to visually verify the registration results. If a large rotation is found, this may be indicative of a failed registration or an incorrect patient set-up. For the former, it may be necessary to repeat the registration with a different setting or starting point. For correctly detected rotations that are out of tolerance, a fresh set-up of the patient may be required.

Prior to treatment delivery the registration should be confirmed as an acceptable representation of the patient set-up. A record of the pertinent aspects of the patient set-up and registration should be kept as guidance for subsequent fractions.

10.2 Brain and central nervous system (CNS) (including stereotactic)

Background	A particular concern with intracranial radiotherapy is the proximity of structures that are particularly sensitive to radiation and where damage with functional loss can have major consequences. Some treatments may require radiotherapy to be planned with steep dose gradients to avoid these critical structures. Effective immobilisation and accurate radiation delivery methods are therefore crucial to provide the higher degree of set-up accuracy required. The optimal timing and frequency of imaging for verification of radiotherapy to the brain is currently undefined. The structure of the head is such that effective immobilisation may result in less patient positional variation than in other anatomical sites and the anatomy of the brain is not subject to large internal motions. Imaging for a minimum of the first three days followed by weekly imaging is recommended to allow adequate assessment of immobilisation and of random and systematic errors.[1,2] Additional uncertainties may occur if the fit of the immobilisation device changes over time (eg, with steroid use resulting in facial swelling). The brain can move very little inside the cranium and the contribution to set-up accuracy from internal organ motion is very small in this group of patients.[3] Thus intrafractional analysis is not required for conventionally fractionated or moderately hypofractionated treatments. However, in fractionated radiotherapy internal brain motion has been reported due to changes in oedema and alterations in the size of the ventricles.[4] Stereotactic radiosurgery (SRS) may be used to treat brain metastases in selected patients as well as benign intracranial conditions. Very high doses are delivered with very steep dose gradients in a small number of treatment fractions (often a single fraction) and with very tight margins (eg, 0–2 mm).[5,6] Extremely high-quality immobilisation and accurate treatment delivery are therefore essential. SRS may be delivered using dedicated systems such as the Gamma Knife or the CyberKnife, or using an appropriately configured linear accelerator.
Patient positioning and reproducibility	The material type used for immobilisation, fixation method, area of material in contact with the patient and supporting technique all affect the achievable reproducibility. Both acrylic and thermoplastic shells may be used and have been shown to result in uncertainties of 3–5 mm.[7–9] Patient compliance may also impact on reproducibility – accuracy may be compromised if the patient is unable to remain still for the treatment duration. This can be due to problems such as neurological deficit, where the patient is physically unable to keep still, nausea from raised intracranial pressure or anxiety. Immobilisation for brain treatments may require whole face masks to be used; this can be problematic in patients with claustrophobia.

	These patients should be identified pretreatment and the problem resolved or the appropriate margins planned and an individual tolerance set rather than conforming to the standard for the technique. Single fraction SRS requires accurate immobilisation. This may include the use of a stereotactic head frame, which results in uncertainties in the region of 1 mm.[10] A head frame is positioned prior to planning and remains on until treatment has been delivered. Alternatively various mask-based systems can be used for SRS, with image guidance to ensure accuracy. This may include image guidance during delivery (intrafraction motion monitoring) for mask-based systems.
Pretreatment imaging	All patients should have a planning CT scan to include the top of the head (beyond the skull) to the foramen magnum or lower border of C3. Intravenous (IV) contrast is not normally required for the CT planning scan but may be of some value for identification of residual disease in patients in whom MRI is contraindicated.[11]
	Co-registration with a recent MRI is required for accurate GTV and OAR delineation. Ideally the MRI scan used should be as close in time as possible to the planning CT (ie, a dedicated planning MRI is preferable, with the patient in a position as close to the treatment position as possible). Where a patient has undergone surgery, use of a postoperative MRI is superior to use of the preoperative MRI as anatomy may have changed in response to surgery. The quality of the co-registration should be confirmed and it should also be confirmed that the anatomy is consistent between both imaging modalities. If marked anatomical discrepancies between the planning CT and MRI are noted (eg, differences in midline shift), an up-to-date MRI should be performed. The sequence used for co-registration is influenced by the clinical scenario. For example, T1 post-gadolinium is usually used to contour the GTV in glioblastoma, while T2 FLAIR is often used to contour the GTV in low-grade glioma. SRS will always involve MRI for target delineation unless there is a specific contraindication. SRS usually employs MRI with 1 to 1.5 mm slice thickness to provide high spatial resolution. Some SRS techniques also require a planning CT scan, co-registered to the MRI. In that case the MRI should include the top of the head (beyond the skull) to facilitate registration.
On-treatment verification	The following workflow is suggested for external beam **non-SRS treatments**:[2,12] ▪ Daily verification may be required for treating tumours planned with very small margins or where patients show inconsistent reproducibility.[13]

- Although an online approach provides optimal accuracy, for other patients an offline correction strategy may still be used.
- Tolerances and action levels to use will vary, particularly with the immobilisation used and compliance of the patient, and should be chosen accordingly.
- Intrafraction verification is unnecessary when delivering conventionally fractionated or moderately hypofractionated external beam treatments.
- Consideration should be given to reducing concomitant exposure when treating benign tumours such as pituitary adenomas, although the need for IGRT may be higher to spare adjacent OAR, in particular if small margins are used. Consider use of low-dose CBCT or kV orthogonal imaging. For whole-brain radiotherapy using a parallel opposed technique, a single 2D image may be sufficient.

SRS

For SRS treatments, image guidance must be performed prior to each fraction, with appropriate correction. For mask-based SRS systems, image guidance during treatment may also be used.[14]

Post-treatment imaging may be used as QA of the procedure.

Site-specific issues

Difficulty in mask fitting: steroid use may make the mask increasingly uncomfortable and difficult to fit, resulting in set-up changes.

Patient non-compliance: patients may find it difficult to remain still due to a neurological deficit, nausea (as a result of raised intracranial pressure) or anxiety. Some patients find wearing a mask or a head frame frightening or psychologically traumatic. Ideally, these patients should be identified pretreatment and the problem resolved or the appropriate margins planned, and an individual tolerance set. As above, cutting out some areas of the mask may be helpful.

Cystic tumours: tumours with cystic components (eg, craniopharyngioma) may cause issues during treatment due to increasing cyst size. This may be detected on CBCT or may be identified through patient symptoms such as increasing headaches and worsening field defects. Repeat imaging to determine if there has been an increase in cyst size may lead to surgical intervention or cyst drainage, which is likely to require replanning. Some advocate routine MRIs (eg, weekly or two-weekly) to assess for cyst progression in craniopharyngiomas where there is a significant cystic residuum.[15,16]

SRS specific issues: for SRS, using a frame-based method can be difficult due to recent craniotomy, in which case a mask-based system may be preferred. SRS can be challenging to deliver safely if the target volume is very close to a critical OAR, particularly the optic tracts.

When treating multiple brain metastases with a single isocentre technique, small rotational errors become more important and rotations should be considered and corrected for. Alternatively a multiple isocentre technique may be used if the distance of the metastases exceeds a certain tolerance. For example, a rotation of two degrees causes a mismatch of 1 mm for metastases that are 5.7 cm apart.

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10.3 Head and neck

Background	Intensity-modulated radiotherapy (IMRT) is now established as a standard of care for treatment of head and neck cancer. Accurate treatment is challenging, with anatomy changes commonly occurring during treatment including weight loss and tumour shrinkage. Steep dose gradients, proximity of target volumes to OAR and recent volumetric outlining guidelines mean that accurate IGRT is essential.[1]
Patient positioning and reproducibility	Patients are immobilised supine in a neutral head position. Consideration can be given to immobilising with a similar neck position to diagnostic imaging prior to radiotherapy to facilitate image co-registration. Use of individualised head rests may be beneficial. A thermoplastic five-point mask is recommended to provide a highly reproducible head immobilisation. A three-point mask likely suffices for treatment confined to paranasal sinuses/skull base. A mouth bite can be considered for some tumour sites (eg, maxillary sinus, floor of mouth) to facilitate sparing of untreated upper/lower jaw. Bolus should be considered for superficial disease.
Pretreatment imaging	IV contrast is recommended to aid target volume delineation and lymph node target outlining; IV contrast may be omitted for treatment of early glottic carcinoma. CT-artefact-reducing algorithms may be useful when dental amalgam interferes with image quality. Co-registration of the planning CT with a positron emission tomography (PET)-CT and/or MRI may be useful in delineation of the target volume if carefully acquired in the treatment position. Fluorodeoxyglucose (FDG)-PET-CT should not be used for delineating tumour boundaries due to lack of spatial resolution.[1] Ideally imaging for co-registration will be obtained in the treatment position not more than four weeks prior to the planning CT. In the absence of treatment-position imaging, rigid co-registration in the ROI or deformable co-registration can be employed with careful visual assessment to ensure adequate registration accuracy.[2] The use of automated segmentation is appropriate if using FDG-PET-CT to guide delineation.[1]
On-treatment verification	Volumetric imaging verification has been shown to be superior to 2D ('planar') orthogonal imaging at detection of shifts and rotational errors.[3,4] 3D imaging is required to detect shifts in primary tumour and lymph node targets that may not correlate with fixed bony anatomy; for example, a study in patients with laryngeal carcinoma demonstrated complex interfractional set-up variation with a lack of correlation in the craniocaudal direction of the primary tumour, lymph nodes and vertebra, in addition to a time-dependent shift in primary tumour target volume craniocaudally.[5] PTV margins need to take account of potential differences in shifts of primary tumour and lymph node target volumes as these cannot be fully accounted for by image-guided correction.[5] Required margins are affected by image quality and larger margins are required with MV-CBCT compared with kV-CBCT.[6]

	In specific cases, positioning of some OAR may be as critical as tumour coverage. Such cases should be identified pretreatment. The optimal frequency of CBCT verification remains a key question. Options for volumetric verification include a 'no action level' protocol of days 1–3 CBCT with offline correction (to account for systematic errors) followed by weekly CBCT (to deal with time trends) or daily CBCT with online correction, which optimises accuracy.[5,7,8–10] Daily CBCT has implications with increased fraction 'on couch' times and is resource intensive. However, several studies have shown that daily imaging verification can be used to reduce residual errors and potentially to allow a reduction in PTV margins.[8,11] Large retrospective studies have suggested that reducing the CTV-PTV margin from 5 to 3 mm with daily CBCT led to a reduction in toxicity without detriment to outcome.[9,12] Daily CBCT with PTV reduction may be of particular clinical value when there is close proximity of target volumes to OAR (eg, locally advanced nasopharynx cancer). In addition, daily CBCT may be advantageous without PTV reduction to ensure target volume coverage in situations associated with greater variability; for example, studies have shown greater interfraction variability for laryngeal/hypopharyngeal carcinoma and in the setting of weight loss during treatment.[5,7,8]
Site-specific issues	In some cases treatment field length will exceed the field of view (FoV) of the imaging system. In such cases an offset may be applied to focus the imaging on the most important region or multiple acquisitions can be stitched together. Anatomical changes during treatment due to weight loss or tumour shrinkage and/or normal tissue changes can cause problems with immobilisation as the mask may not fit well due to the change, and this can lead to deviations of delivered dose from planned dose. Rigorous pretreatment dietetic assessment and ongoing support throughout treatment is essential to minimise weight loss. ART with replanning part way through treatment may be required to correct for anatomical changes to ensure target volume coverage/OAR sparing. Due to the use of the PTV, the CTV is generally more robust to dosimetric impact of anatomical changes compared with OAR.[13] A multitude of pretreatment and on-treatment factors have been suggested as criteria for ART in a range of heterogenous studies.[13] For example: on-treatment factors include weight loss and tumour volume decrease, which correlate with spinal cord dose; lateral dimension changes with mucositis; and weight loss, reduction in lateral neck diameter, parotid gland volume decrease and tumour volume shrinkage potentially increase parotid gland dose. However, ART is resource intensive and the optimal indications, frequency and clinical benefit of ART remain uncertain. A recent study failed to show a useful benefit of routine mid-course CT-based dose verification in the presence of daily CBCT verification.[10] At present the evidence base does not justify an approach of routine ART for all patients.

ART needs to be considered on an individual basis when anatomical changes during treatment/inconsistent set-up raise concern for target volume coverage and/or excess OAR doses. Due to a potential lack of correlation between the primary tumour and nodes, ART will be required if CTVs are found to drift out of PTV on CBCT.[5]

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10.4 Breast

Background	Treatment verification during breast radiotherapy increases the accuracy of treatment delivery. MV portal imaging has been the mainstay of reproducibility assessment when delivering whole-breast radiotherapy with tangential fields. There is evidence that for standard open tangential field MV, portal imaging remains an option but when compared with more complex IGRT techniques, such as CBCT registration, MV portal imaging has greater residual errors.[1] The implementation of more conformal radiotherapy such as IMRT and VMAT along with the increasing role of simultaneous integrated boost (IMPORT HIGH) and partial-breast radiotherapy (IMPORT LOW) may necessitate the use of more sophisticated localisation and verification techniques.
Patient positioning and reproducibility	The use of commercial or custom-made breast boards with adjustable arm rests for treatment in the supine position can achieve effective immobilisation for breast radiotherapy. Reproducibility is improved with the use of knee rests and bottom support to prevent slippage down the board. Positioning with both arms up is more stable. Additional immobilisation devices include Alpha Cradle and vacuum bags. The choice of immobilisation used will affect set-up reproducibility. With the above set-up techniques, population systematic and random errors have been shown to be in the range of 2.1–6.5 mm.[2] The use of cardiac sparing techniques should be adopted for left-sided breast irradiation to minimise cardiac dose and long-term cardiac toxicity. This is particularly important when an unacceptably high heart dose would otherwise be delivered, such as when including the internal mammary chain. This can be effectively achieved using breath-control techniques, in particular voluntary DIBH or active breath control.[3,4] Coaching prior to simulation is critical to optimise reproducibility of breath-hold, particularly for DIBH. DIBH can be monitored during treatment using closed-circuit television images. Respiratory gating techniques are also helpful to achieve cardiac sparing. Patients with pendulous breasts may benefit from other forms of immobilisation such as thermoplastic shells, wireless bras or breast cups. Treatment in the prone position may also be advantageous although reproducibility of treatment remains inferior to that in the supine position.[5]
Pretreatment imaging	Use of IV contrast can be advantageous where delineation of nodal volumes is required. Marking a breast CTV is difficult on CT images and there is considerable inter-clinician variability.[6] In view of this, anatomical borders are commonly used to determine breast, chest wall and nodal fields, creating consistent volumes that can be used for plan evaluation.

If a whole-breast CTV is to be marked, wiring of palpable breast tissue before scan acquisition can be helpful. Typical expansion to PTV would be 10–15 mm, but centres should decide a growing margin appropriate for their equipment and tolerances.

The British Association of Surgical Oncology recommends insertion of clips to delineate the tumour bed following breast-conserving surgery.[7] Guidelines for a reproducible method of clip insertion were produced by the IMPORT Low team.[8] These clips aid both accurate tumour bed localisation and pretreatment verification and are of particular importance for partial-breast radiotherapy.

For partial-breast radiotherapy or boost, the tumour bed should be delineated. The CTV should include the clips and surrounding postoperative changes with a 5 mm margin.[9] CTV-PTV margins should be between 5–10 mm depending on local population systematic and random error calculations.

Nodal fields are traditionally marked using anatomical borders, but 3D delineation of nodal levels is increasingly being adopted as a standard of care.[9] This brings improved confidence in adequate dose delivery to nodes, particularly in patients with a wider separation and when the axilla is being treated. Instruction in nodal and OAR (brachial plexus) delineation can be found in the ESTRO guidelines.[9]

On-treatment verification

Light field visualisation along with skin distance measurement can be used to assess patient set-up, for simple whole-breast tangential field radiotherapy. However, this is insufficient to assess OAR overexposure and additional image-based verification is required. It is common for small adjustments to be made to the set-up to ensure clinical coverage of the breast and concordance with the planned field.

Electronic portal imaging (EPI) of the tangential beam can be used to measure the central lung distance and will demonstrate if lung tissue is being overexposed. Registration of the portal image to the pretreatment DRR can be performed using bony anatomy (ribs) and breast contour. Central lung depth, anterior flash distance and inferior central margin are used to estimate field accuracy. Michalski *et al* found inter/intrafraction motion in whole-breast radiotherapy measured with EPI to be around 5 mm.[10] EPI of tangential fields, however, does not allow for the assessment or correction of errors in the three cardinal directions (longitudinal, lateral and vertical) and is known to under-report any longitudinal error when compared with other imaging techniques.[1] Therefore, a larger CTV-PTV margin of 10–15 mm is required.[1] Despite the limitations of EPI, there is no evidence of benefit of volumetric IGRT in tangential whole-breast radiotherapy and this remains the imaging modality of choice.[12] This can also be used for simple IMRT where a combination of open and segmented fields is used.

kV imaging: when conformal target volumes using tighter CTV-PTV margins are required (partial-breast irradiation, simultaneous integrated boost or sequential photon boosts) IGRT is recommended. This is also the case for more complex radiotherapy delivery techniques (IMRT and volumetric modulated arc therapy (VMAT)).

Use of kV imaging allows accurate determination and correction of set-up errors in all three cardinal directions. This makes it possible to decrease the CTV-PTV margin to <10 mm. Each centre should determine its own population systematic and random error for margin calculation.

Paired kV imaging and kV/MV imaging: paired kV imaging for breast treatments has been demonstrated to be an efficient IGRT technique.[13] Orthogonal or near-orthogonal paired images are taken after the patient is set up and these images are registered to bony anatomy on the corresponding DRR from the planning CT (ribs, sternum and vertebrae).

Matching to tumour bed clips has proven to be more accurate when compared with a bony landmark match alone. In this situation tumour bed boost CTV-PTV margins can be reduced from 8 to 5 mm.[13] Paired kV/MV imaging, where the MV imaging coincides with the treatment field and can be accounted for in the treatment plan, may be considered as an alternative.

CBCT: image registration using bony anatomy and surgical clips maximises set-up accuracy and allows optimal localisation of the tumour bed.[12] With this technique residual error has been shown to be as low as 1.6 mm.[14] There is no clear evidence that achieving this level of accuracy gains a clinical advantage over paired kV imaging. Furthermore, CBCT can be difficult to acquire in situations that require active breath control. When soft-tissue anatomy needs to be visualised, such as for a changing seroma, CBCT can be helpful. Imaging dose to the contralateral breast should be kept to a minimum.

IGRT protocol

In most situations the following protocol is acceptable:

Daily pretreatment imaging fractions 1–3 with online correction for gross error shifts.

Fraction 4: calculate mean error from fractions 1–3 and apply this correction to isocentre position, followed by pretreatment verification.

If set-up is within tolerance, continue treatment with weekly imaging.

A suitable tolerance for errors is 5 mm. If errors are larger than this then the set-up should be checked and if the error cannot be resolved (with an imaging correction protocol) then resimulation or replanning is advised.

Daily imaging with online correction is required when there are errors that cannot be resolved or when hypofractionation protocols are being used.

Site-specific issues	Optimal immobilisation with both arms up can be challenging in larger patients even with wide bore simulators. While only a limited CBCT arc (200 degrees) is required, this can be difficult to achieve in some patients due to collision with the arm rest. The time taken for scan acquisition can be challenging for patients in breath-hold. It has been demonstrated that breast volume changes occur during treatment and therefore should be considered for any dosimetric consequences. Where there is evidence of a resolving seroma, resimulation may become necessary, particularly for treatments involving tumour bed boost.

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10.5 Lung

Background

The delivery of accurate radiotherapy to tumours arising in the lung poses a series of complex challenges to clinical departments.

IGRT in lung cancer is accepted as standard. Studies have demonstrated that the use of IGRT improves patient positioning and provides improved geometric and dosimetric conformance with the intended treatment plan.[1,2] IGRT is also beneficial when the intention is to minimise dose to OAR, which may influence morbidity and mortality.[3]

Studies in lung cancer radiotherapy have demonstrated significant inter-observer variation in GTV delineation.[4] This variation can be minimised by incorporating additional pretreatment imaging such as PET-CT or MRI fusion into the planning process.[5] It can be particularly helpful in defining the GTV in areas of lung collapse.

At the stage of treatment delivery, IGRT can verify the tumour and/or OAR position, such that subsequent actions may be able to improve or verify the accuracy of the treatment. There are, however, some specific challenges inherent in IGRT for tumours contained within the lung.

- Tumours within the lung can be difficult to see with 2D planar imaging.
- Tumours within the lung can move significantly through respiration and other influences (baseline motion).
- During treatment, changes in the external (eg, weight loss) and internal anatomy (eg, tumour increase/decrease, collapse or reinflation of the lung) occur often.

A very significant component of lung IGRT to address is tumour motion. Tumours within the lung can move independently of bone anatomy. To deliver the radiotherapy accurately, the tumour must be imaged directly using volumetric imaging or a surrogate. For node-negative early-stage tumours, implanted fiducial markers or transponders can be used as a surrogate.[6] For more advanced tumours, bone or carina can be used as a surrogate to ensure tumour and nodal coverage.

Internal organ motion during the respiration and cardiac cycle presents a particular challenge for ensuring accurate thoracic radiotherapy. For patients with significant tumour movement (>1 cm) motion management strategies can be used. There are a number of methods to minimise the influence of tumour and/or OAR movement during radiotherapy. The optimal strategy to employ is multifactorial and department specific.

Potential strategies may include breath-hold techniques, gating based on external and internal surrogates, accounting for motion when defining radiotherapy target margins, 4D image guidance and abdominal compression.[7]

The method of IGRT required may depend on the treatment intent, the size of the PTV margins planned/needed and the fractionation schedule.

SABR

Lung SABR is the delivery of high-dose hypofractionated radiotherapy to tumour(s) within the lung.[8,9] Lung SABR is recommended as the standard of care for the management of early-stage medically inoperable peripheral non-small cell lung cancer.[10] The delivery of such large ablative doses requires high levels of precision and accuracy to maintain small margins around the tumour and rapid dose falloff. High-quality IGRT and immobilisation are therefore essential.[11] The UK SABR Consortium Guidelines, intended to ensure safe implementation of SABR delivery, provide considerable practical guidance on the clinical implementation of lung SABR.[12]

Patient positioning and reproducibility

Accurate positioning can be achieved using rigid immobilisation systems such as wing, thoracic or breast boards. The arm position can be above the head but can also be at the patient's side immobilised in a thermoplastic shell. The latter option is most often employed in the treatment of apically located lung tumours (eg Pancoast/superior sulcus tumours), though it can be used for any patient if preferred, particularly for patient comfort during time-consuming procedures.

Palliative treatments may require a greater level of patient comfort. Patients who are in pain, breathless or emaciated are more likely to suffer from discomfort during radiotherapy planning and treatment, which may manifest in an increased risk of movement. Soft couch materials and a higher gradient of elevation should be considered as these may be sufficient to enable the patient to maintain the treatment position for the duration of treatment.

Indexed knee supports improve patient comfort and treatment reproducibility by increasing the surface area contact of the patient to the couch and reducing the chance of rotation. These should be employed in radical and palliative cases.

SABR treatments will require high levels of treatment accuracy and immobilisation may therefore be extended either by adapting the current system (eg, adding a customised vacuum bag or chin strap) or using specific SABR immobilisation devices and thermoplastic shells. However, patient motion is limited when procedures are fast, and with flattening filter-free VMAT, image guidance may be used without extensive immobilisation.[13]

Pretreatment imaging	For palliative lung radiotherapy, a CT planning scan is highly recommended. For radical lung radiotherapy CT planning is required, with IV contrast offered to all patients with tumours close to or involving the mediastinum (including nodal disease) and for those tumours close to the brachial plexus unless contraindicated. The use of contrast improves delineation of mediastinal structures, brachial plexus and distinguishing the tumour from consolidation. 4D CT should be used to account for tumour motion and minimise artefacts stemming from motion when the motion amplitude exceeds 5 mm. The 4D CT can be used to estimate the magnitude of breathing motion. How the 4D CT is used will depend on the choice of motion management strategy employed (eg, average position/mid-ventilation approach or ITV approach). The planning data set should ideally be a mid-ventilation or average data set if obtainable from the 4D CT system. If not obtainable, a standard 3D free-breathing CT or an additional breath-hold CT can be acquired to aid target delineation (and minimise movement artefacts further). However, it should be acknowledged that in such scans the position of the tumour may deviate relative to OAR compared with free breathing due to image distortion (3D scan) and/or unrepresentative breathing state. If respiratory gating is being used, the phase of the 4D CT suitable for gating must be used as the planning scan. This is often the end-expiration phase (high stability and large fraction of time spent in gating window) but in some cases the inspiration phase may be felt optimal for gating. If a breath-hold technique is being used, the pretreatment imaging scan is obtained in breath-hold. To improve accuracy of delineation of GTV, fusion with MRI or PET can be considered.[14–15] To allow accurate fusion to aid delineation of ITV, the PET or MRI should be acquired in the radiotherapy treatment position and fused with the AIP. The limitations of this registration must be appreciated. Typically use PET or MR to identify regions and CT to define boundaries.
On-treatment verification	**Palliative lung radiotherapy** Generally for short-course palliative lung radiotherapy larger margins are used to account for set-up uncertainty. As such a bone match is considered a reasonable surrogate. Planar imaging can be used for detection of gross and systematic errors. For more complex palliative treatment where OAR tolerance may be an issue then volumetric online matching may be required. Some departments solely rely on volumetric imaging, and these should also use volumetric imaging for palliative treatments.

Radical and high-dose palliative lung radiotherapy

Volumetric imaging (CBCT) is considered the standard of care for radical and high-dose palliative treatment plans.[16,17] The use of cone-beam CT scans allows more accurate set-up over portal imaging.[16] Daily image guidance with soft-tissue set-up to primary tumour or anatomical landmarks is recommended.[16,18] Mediastinal lymph nodes are more difficult to visualise on CBCT and, if needed, anatomical landmarks or surrogates should be used for matching. Daily CBCTs and set-up corrections allow the use of smaller CTV to PTV margins by reducing systematic and random errors.

4D CBCT, if available, is superior to 3D CBCT in image guidance in small lung tumours with peak–peak motion of 1 cm or over, reducing the uncertainty of tumour location.[19] Images should be assessed online for random and systematic errors and corrections made in line with departmental protocols, taking into account CTV to PTV margins. Corrective shifts that could impact on doses to OAR should be evaluated. The acquired images should be assessed for changes to the target volume and surrounding tissues when compared with the pretreatment planning images. An assessment should be made as to whether any changes may affect the planned treatment.

Offline assessment of images may require an MDT discussion to assess any perceived changes to the target volume and surrounding tissues that may have a dosimetric impact on the proposed treatment plan. The MDT may recommend a treatment replan (see Section 7 Adaptive radiotherapy). In addition, it is important to detect important anatomical changes such as pleural effusion, consolidation and lung collapse and request medical evaluation if deemed necessary according to local protocol.

Lung stereotactic ablative radiotherapy (SABR)

Online image guidance is essential for every treatment fraction of lung SABR. For efficient and accurate delivery of SABR it is essential to use decision-making protocols. Potential problems necessitating multidisciplinary assessment for clinical and dosimetrical impact are:

- Large systematic or random errors
- Significant contour changes
- Significant soft-tissue changes (tumour or local lung tissue)
- Larger than expected tumour motion
- Baseline shifts.

	Given the large doses per fraction, therapeutic radiographers are advised to use caution as necessary and seek additional advice in the case of any uncertainty, especially if there is a risk of overexposing nearby OAR due to relative motion of the tumour or if the tumour is poorly visible. The recommended workflow for lung SABR IGRT is to acquire an initial verification image, perform image registration and online correction using appropriate action levels and repeat imaging depending on the action level (eg, large displacement) or if there are concerns about patient movement. The use of 4D CBCT should be considered to ensure the tumour and/or OAR motion is consistent with the treatment plan. 4D CBCT is particularly useful in lower lobe tumours given the proximity to the diaphragm. Intrafraction imaging/monitoring can be used, in particular for SABR treatments that take longer to deliver with evidence of intrafraction tumour deviation for treatment longer than 30 minutes.[20] Post-treatment imaging can be used as a QA method for the entire workflow, particularly on implementation and revision of SABR workflows.
Site-specific issues	Changes in anatomy are observed commonly during a course of thoracic radiotherapy, which can be transient or persistent.[17,21] Persistent changes such as weight change, pleural effusion and atelectasis can lead to changes in anatomy. This can lead to changes in dose to PTV and/or OAR. Such changes need to be assessed during treatment and the radiation plan adapted as required. Each individual centre will need to consider an appropriate action for replanning based on their current resources and this needs to be decided with the clinical oncologist and medical physics team. Some visible changes may require medical intervention.

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10.6 Gastro-oesophageal

Background	With gastro-oesophageal cancers it can be challenging to define the GTV and loco-regional lymph nodes, which are affected by respiratory and peristaltic organ motion. Multi-modal imaging is therefore used to help define the GTV including PET/CT and endoscopic ultrasound. For lower oesophageal and stomach cancer, respiratory motion can affect the tumour position and the stomach can change size due to gastric filling.
Patient positioning and reproducibility	Patients undergoing radiotherapy to the stomach or oesophagus should be positioned supine in a reproducible position using an immobilisation device such as a wing board and/or vacuum bag and a knee block for comfort. Ideally their arms will be raised above their head, unless a proximal oesophageal cancer is being treated. In that case patients should be scanned with arms by their side, using a knee support and immobilised in a five-point shell. The lower section of the oesophagus is the most mobile, particularly in the craniocaudal direction, due to respiratory motion. The use of 4D CT for radiotherapy planning should be considered for tumours of the lower oesophagus, gastro-oesophageal junction and stomach with the aim of individualising treatment volumes and ensuring adequate tumour coverage. Reported studies assessing respiratory motion provide recommended margins for treatment where 4D CT is not available.[1] For patients with stomach cancers it has been found that intrafraction motion can occur in the range of 1–3 cm and interfraction variation due to gastric distention can occur in the range of 3–5 cm.[2] A fasting protocol helps to improve consistency of gastric filling.[3] These variations in stomach position and shape should be considered in all treatment planning and verification processes.
Pretreatment imaging	**Imaging modalities:** to define the target volume in gastro-oesophageal cancer, clinical information from all staging modalities is used (diagnostic CT scan, endoscopic ultrasound (EUS) and PET-CT). The use of PET-CT for GTV delineation in radiotherapy planning can help increase the accuracy compared with CT alone, though further work is required to standardise the use of PET-CT and ensure reproducibility.[1] PET-CT tends to underestimate length of disease compared with EUS, risking geographical miss if EUS is not available.[4] As a minimum an IV contrast-enhanced 3D CT scan should be obtained, followed by a 4D CT if appropriate.

	Scan limits: scan limits will vary depending on the location of the disease or, in the postoperative setting, the tumour bed. For upper and mid-oesophagus tumours 4D CT is not mandated. As a minimum the planning CT for gastric cancers should cover the abdomen and lower chest, including the pancreas, liver and kidneys. For oesophageal cancers it is important that the full lung volume is scanned. For example, from 1 cm superior to the lung apices or 6 cm superior to proximal disease extent (whichever is higher) and inferiorly to the bottom of L4.[3] **Contrast:** IV contrast, unless contraindicated, can be used to aid target delineation for gastro-oesophageal tumours. For lower 1/3 gastro-oesophageal junction and stomach tumours, patients should fast for two hours prior to their planning scan and each treatment delivery, unless this is not possible for medical reasons. Patients should drink, for example, 200 ml of water 30 minutes prior to a CT planning scan and prior to delivery of each fraction of radiotherapy. The same stomach preparation procedure should be followed before planning and each treatment with the aim of reproducible stomach filling.[3] An oral contrast (eg, dilute gastografin) can be used to help with tumour visualisation for patients undergoing gastric radiotherapy. This can be administered 15 minutes prior to CT imaging. **Reference tattoos:** anterior and lateral alignment tattoos should be used to aid set-up and avoid rotation. Fiducial markers or surgical clips may be used as reference points as per institution practice. Endoscopically placed clips may be helpful to define the proximal and distal margins of early gastro-oesophageal tumours not visible on CT or PET imaging.[5]
On-treatment verification	For linac-based treatments, patients should follow the same fasting/drinking protocol as for pretreatment. A CBCT or 4D CBCT imaging (if there is significant motion) should be performed.[6] An initial bony registration should be done and then the oesophagus and oesophageal tumour position should be checked. The sagittal reconstruction is usually the best way to visualise the oesophageal tumour and oesophagus but all other views should be reviewed. Surrounding soft-tissue anatomy can be used either with automatic dual registration or manual adjustment to ensure the tumour(s) is encompassed within the PTV. The following may be helpful. Carina can be used as a surrogate for tumour position in mid-oesophageal tumours.[7] Surgical clips may be useful for matching in postoperative radiotherapy.

	Imaging frequency: the minimum requirement is imaging pretreatment on days 1–3, then weekly. Daily imaging should be considered for all patients and particularly in cases with set-up issues or concern about proximity to critical OAR structures.
Site-specific issues	Weight loss can be an issue and therefore nutritional support is recommended. Prophylactic anti-emetics (eg, ondansetron) may be required, depending on the amount of gastric tissue within the treatment field. Oesophageal positioning and tumour volume changes should be assessed, and adaptive planning should be considered.[8] When patients are receiving induction chemotherapy prior to planned definitive chemoradiotherapy, the radiotherapy planning scan should ideally be performed within the first two weeks of induction chemotherapy.[3] It can be difficult to deliver a substantial radiation dose to the oesophagus and stomach without excessive radiation doses to the heart, lungs, kidneys and spinal cord. However, use of image-guided IMRT and VMAT can allow better dose coverage, including the possibility of dose escalation.[9]

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10.7 Hepato-biliary

10.7.1 Liver (including primary and metastatic)

Background	Target delineation, image guidance and treatment delivery are challenging in liver radiotherapy due to factors including respiratory motion and difficulties visualising the tumour on a standard contrast-enhanced CT or non-contrast CBCT. Multi-modal, and often multiphase, contrast-enhanced imaging is therefore needed during treatment planning. Strategies to minimise and validate respiratory motion should be employed.[1,2]
Patient positioning and reproducibility	Patients undergoing liver radiotherapy should be positioned supine in a reproducible position using an immobilisation device such as a wing board and/or vacuum bag and a knee block for comfort. Ideally their arms will be raised above their head, in a suitable immobilisation device. Respiratory motion should be quantified and all motion >5 mm should be managed as appropriate to resources and experience. The amplitude of respiratory motion may be assessed by kV fluoroscopy, 4D CT or cine-MRI. All motion management strategies should be validated locally, particularly the patient reproducibility of breath-hold techniques.[3,2] When using abdominal compression with a compression plate avoid treatment delivery through the compression plate whenever possible. Alternative abdominal compression systems (eg, dosimetry using belted devices) may not be affected and treatment can be delivered through the belt.
Pretreatment imaging	**Imaging modalities:** it is often challenging to delineate primary liver cancers for treatment planning and the involvement of a specialist hepato-biliary radiologist for contouring guidance/review is strongly encouraged. Diagnostic imaging can be reviewed to help select the optimal phase in which to acquire a planning scan. Many primary liver cancers are better visualised in the arterial phase and/or delayed phase, but a portal venous phase may be needed in addition (eg, to determine the extent of any tumour vascular involvement). FDG-PET can lead to an increased or decreased GTV to be delineated when merged with CT and/or MRI. However, incorporating PET for radiotherapy planning has not yet been validated. PET may be useful in determining GTV in previously treated liver tumours, where it is able to more accurately differentiate an active tumour from scar tissue.[4] **Scan limits:** to cover the entire liver plus >2 cm in both the superior and inferior extent, as well as OAR.

	Contrast: contrast-enhanced CT (CECT) should be used to outline GTV. Ideally dynamic contrast-CT in exhale breath-hold, which allows better visualisation of the upper abdominal organs, should be used to capture the appropriate phase of contrast enhancement for the tumour type being treated. For those patients who do not tolerate breath-hold techniques or abdominal compression, 4D CT may be used to estimate tumour motion. Contrast-CT fused with treatment-position MRI should be considered and used if available because CECT can underestimate liver metastases.[5] T2w non-contrast-enhanced imaging and/or gadolinium-based contrast-enhanced T1w imaging covering the entire liver is recommended. As a minimum, a diagnostic MRI should be obtained and used to inform target delineation unless contraindicated.[6] Patients should fast for two hours prior to their planning scan and each treatment delivery, unless this is not possible for medical reasons. Patients should drink 125–200 ml of water (or dilute gastrografin contrast) approximately 15 minutes prior to scanning. This aids visualisation of the upper gastrointestinal tract and should be repeated prior to each treatment to maintain reproducibility. Fiducial markers or surgical clips may be used as reference points as per institutional practice.
On-treatment verification	Fasting and use of oral contrast/water prior to each fraction should be the same as for treatment planning to maintain reproducibility. For online CBCT or 4D CBCT imaging commence with bony alignment initially. Subsequently, for CBCT, use the diaphragm/whole liver as a surrogate for the tumour, or if MRI is being used on the treatment machine this can be used to match the tumour. When whole-liver registration (as a surrogate for tumour position) cannot be achieved satisfactorily, registration in the region of the tumour should be favoured. Position of dose limiting OAR should be considered also. When using breath-hold treatments, depending on the length of image acquisition and breath-hold, the CBCT acquisition can be paused and restarted. Liver motion should be reviewed (eg, on a 4D CBCT as above for free breathing or abdominal compression). Adjustments to the compression device or breathing coaching may be needed. It is important to verify breath-hold reproducibility before and during radiotherapy. Alternatively, register to fiducial markers or surgical clips if present. Because of the low soft-tissue contrast of liver tumours, MRI-guided radiotherapy is a promising technique for liver cancers, using the MR for localisation, gating and intrafraction motion monitoring.[7]

	Imaging frequency: as a minimum, daily online imaging is required, with repeat imaging following major shifts. For centres validating this process, a repeat CBCT at the end of the fraction has been recommended by commissioning through evaluation SABR.[8]
Site-specific issues	As noted above, the target lesion is often not easily visible on CECT or CBCT, and as such use of surrogates for matching during image guidance is frequently required. A change in the breathing pattern of the patient between planning and treatment visits can lead to excess movement of the tumour outside of PTV if the respiratory amplitude is greater. This issue needs to be considered.

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10.7.2 Pancreas

Background	Target delineation, image guidance and treatment delivery are challenging in patients with pancreatic cancers mainly because of respiratory and bowel motion affecting the visibility of the target. Strategies to minimise respiratory motion are helpful to improve image quality and therefore target localisation. However, the reproducibility of such techniques must be validated.
Patient positioning and reproducibility	Patients undergoing radiotherapy to the pancreas should be positioned supine in a reproducible position using an immobilisation device such as a wing board and/or vacuum bag and a knee block for comfort. Ideally their arms will be raised above their head. A fasting protocol helps to improve consistency of gastric filling. Respiratory motion management strategies such as abdominal compression or breath-hold techniques can be considered.[1–4]
Pretreatment imaging	**Imaging modalities:** an exhale breath-hold contrast-enhanced 3D CT followed by a 4D CT. Ideally a 4D CT is obtained to define the ITV taking into account individualised tumour motion during the breathing cycle.[5] The exhale phase of the 4D CT will be registered with the contrast-enhanced 3D exhale breath-hold CT. An exhale breath-hold 3D scan is preferred as it enables better upper abdominal organ visualisation than a free-breathing CT. If a patient cannot achieve exhale breath-hold, or a 4D CT cannot be obtained, then a free-breathing contrast-enhanced 3D-CT should be acquired.[5,6] **Scan limits:** from at least 5 cm above the dome of the diaphragm to the inferior aspect of the L4 vertebra to ensure all OAR (liver, stomach, duodenum, small bowel, kidneys) are included in the scan.[6] **Contrast:** IV contrast, unless contraindicated. Patients should fast for two hours prior to their planning scan and each treatment delivery, unless this is not possible for medical reasons. Patients should drink 125–200 ml of water (or dilute gastrografin contrast) approximately 15 minutes prior to scanning. This aids visualisation of the upper gastrointestinal tract and should be repeated prior to each treatment to maintain reproducibility.[6] Fiducial markers may be used as reference points, more commonly with SBRT.[7,8]

On-treatment verification	Fasting and use of oral contrast/water prior to each fraction should be the same as for treatment planning to maintain reproducibility. **Online CBCT or 4D CBCT imaging:** a particular advantage of breath-hold techniques is that they resolve the image blurring due to respiration and improve visualisation of fatty tissues surrounding the pancreas.[9] Confirm that the target structure to be used for registration (identified from a local protocol such as CTV) falls within the volume created (eg, ITV) to encompass the motion identified at the time of simulation. Surrounding anatomy can be useful in the manual adjustment to ensure the target is encompassed as prescribed using the following. ▪ Calcifications in the abdominal aorta can provide a good surrogate matching point in all three planes. ▪ The duodenum can aid in matching the superior/inferior position of the pancreas (especially if patients have had water/oral contrast immediately prior to set-up). Note: ▪ Biliary stents are *not* a reliable surrogate for matching.[10,11] ▪ Matching can be challenging and therefore it is recommended to review each case in an MDTM to decide on an imaging strategy for each patient before treatment. **Imaging frequency:** the minimum requirement is daily imaging pretreatment on days 1–3, then weekly. Consider daily imaging for SABR and issues with set-up or concern about proximity to critical OAR structures.
Site-specific issues	Bloating and excessive gas production can occur as a result of pancreatic exocrine insufficiency in patients with pancreatic cancer. Many patients will be prescribed pancreatic enzyme replacement therapy (eg, Creon) and ideally should have optimisation of dosage prior to radiotherapy. Excess gas that is mobile and free breathing can pose a challenge in obtaining good-quality CBCT images (see example in Section 10.7.2, Appendix 14.5) and occasionally in ensuring adequate tumour coverage and dose distribution is achieved. Weight loss can be an additional issue in this patient group.

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10.8 Colorectal/anal

10.8.1 Rectum

Background	The majority of rectal motion is interfraction motion between radiotherapy fractions. Rectal lumen size, due to gas and faecal matter, can differ day to day. In addition, bladder filling varies and can affect the position of the rectum. The site and fixity of the tumour are the main factors that predict the likelihood of motion with recent evidence confirming the most marked movement is of the resectable upper rectal tumours and during the first week of treatment.[1,2,3] If a stoma is present, there will be less distortion of the rectal lumen by gas and faecal material. IMRT is now in use with doses >50 Gy and as such IGRT strategies for delivery in this setting must be used.[4,5,6]
Patient positioning and reproducibility	Patients should be treated supine with immobilisation for popliteal fossa and/or feet. With standard conformal treatment to 45–50 Gy, patients can be treated prone with the use of a bellyboard. The disadvantage is the slight reduction in stability when compared with supine and the disadvantage is the discomfort, especially for male patients and those with a stoma.
Pretreatment imaging	Patients should be scanned with a comfortably full bladder. Patients should be encouraged to empty their bowel prior to scan. If the rectum is very full, enemas or laxatives can be prescribed. Intravenous contrast is recommended to allow identification of the vasculature. Oral contrast is recommended to assist with the delineation of the small bowel. An anal marker at the anal verge can aid identification of the inferior edge of the tumour with the use of endoscopic and clinical findings. The scan parameters should include the superior aspect of L3 to below the anal marker or the inferior aspect of the tumour marker, whichever is lower. The CT planning scan should be reviewed in conjunction with the diagnostic MRI, ideally fused within the planning system.
On-treatment verification	**3D CRT:** use orthogonal planar imaging or CBCT images on fractions 1–3 and weekly with calculation of systematic error and shift if required. Matching is to bony landmarks. CBCT should be assessed for coverage of all soft-tissue CTV targets. **IMRT/VMAT:** CBCT should be performed at a minimum on fractions 1–3 and weekly thereafter. On other fractions, at least planar imaging should be used. Matching performed is to bony landmarks. CBCT should be assessed for coverage of all soft-tissue CTV targets.

	Daily imaging should be considered where justifiable for all patients. Registration to the target is recommended provided assessment of nodal coverage is performed and changes are made as appropriate. It may be appropriate to consider a bony match where there are involved nodes.
Site-specific issues	**Achieving a consistent bladder volume:** if bladder volume is reduced from the planning scan, encourage drinking for subsequent fractions. Consider use of a bladder scanner if available. If reduced bladder volume is consistent over several fractions a replan may be considered to reduce dose to the bladder and small bowel, which with a smaller bladder may have moved into the original CTV target. Bony match will cover pelvic nodes well; however, the primary tumour may move independently to this. As such it is necessary to check primary tumour coverage following bony match to ensure all targets are covered adequately.

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10.8.2 Anus

Background	Most anal squamous cell cancers are usually treated with IMRT unless radiotherapy is used to treat a very early-stage tumour. An anal IMRT/VMAT plan has three distinct targets that move separately to one another: primary anal tumour, inguinal nodes and pelvic nodes; however, they are treated in a single plan with a single set-up.[1,2]
Patient positioning and reproducibility	Patients should be treated supine with immobilisation for popliteal fossa or feet.
Pretreatment imaging	Patients should be scanned with a comfortably full bladder and bladder ultrasound can be used to verify bladder status prior to CT scanning. Intravenous contrast is recommended to allow easy identification of the pelvic vessels. Oral contrast is recommended to assist with the delineation of the small bowel. An anal marker can be helpful and would be placed at the anal verge or around the anal tumour if it extends beyond the anal verge. However, caution is needed as the marker position can change with respect to the tumour. The scan parameters should include up to L4 superiorly and 5 cm below anal margin or gross tumour, whichever is more inferior. The CT planning scan should be viewed with diagnostic MRI and PET, ideally with the images imported into the planning system.
On-treatment verification	**IMRT/VMAT:** online CBCT should be performed at a minimum on days 1–3 and weekly thereafter. On other treatment days, planar imaging (matching to bony landmarks) can be used, though daily imaging with CBCT should be considered for all patients. CBCT matching to primary tumour target is appropriate provided assessment of inguinal and pelvic nodal coverage is performed and changes are made as required. It may be appropriate to consider a bony match where there are involved nodes. CBCT should be assessed for gross soft tissue coverage and changes over time.

Site-specific issues	If bladder volume is reduced from the planning scan, small bowel dose may be increased and therefore bladder volume control should be considered as above (see Section 10.8.1). Irradiation after bony registration will typically cover pelvic nodes; however, the primary tumour may move independently to the nodes. As such, it is necessary to check primary tumour coverage following bony match to ensure all targets are covered adequately. Due to the field length it may not be possible to visualise the whole treatment volume of the CBCT scan. Whether using bony or soft tissue match, care must be taken to ensure coverage of other targets, namely inguinal and pelvic nodes and the primary tumour, and adaptations made as appropriate.

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10.9 Gynaecological

Background

IGRT protocols for gynaecological cancers vary depending on the indication for treatment and the target structures. Broadly, these can be defined as tumour targets including the intact uterus (eg, primary radiotherapy for cervix cancer) or the postoperative pelvis (eg, after hysterectomy as adjuvant therapy for endometrial or cervical cancer).

IMRT/VMAT is routinely delivered for female pelvic targets, improving conformity and reducing dose to normal tissue, but the accuracy of treatment delivery is reduced by geometric uncertainty. The sources of this uncertainty are multifactorial:

- Inter- and intrafraction motion of targets caused by substantial changes in bladder and rectal volume[1,2,3]
- The CTV may involve multiple structures, which move independently of bony anatomy and each other
- Extended pelvic fields, which are highly susceptible to rotational set-up error
- Tumour regression during treatment (eg, with cervix tumour regression of 50 per cent.[4,5]

IGRT protocols that visualise soft-tissue targets at the time of radiotherapy are key to minimising these uncertainties.

Target motion

Significant position and shape variations in cervical cancer CTV anatomy, including uterus, cervix and upper-vagina, occur during radiotherapy naturally or due to changes in bladder, rectal and tumour volume.[1,2,6,7] Insufficient CTV coverage occurs even with large CTV to PTV margins, resulting in target under-dosing or overdosing of normal tissue. Motion is greatest at the uterine fundus (frequently included in a cervical cancer CTV, but under discussion), up to 32 mm in a superior/inferior plane and 48 mm in an anterior/posterior plane.[8] The cervix itself is subject to less motion but margins up to 30 mm may still be required.[9]

Radiotherapy to the postoperative female pelvis includes the pelvic lymph nodes and vaginal vault. The central vault target is subject to motion influenced by rectal and to a lesser extent bladder filling. Extent and variability in target CTV is largest in the anterior/posterior direction with displacements of up to 30 mm observed.[10–13] This means that even with a standard CTV-PTV margin of 15 mm, dosimetric insufficiency would often occur.[14] For this reason, ART can be used to reduce margins and/or avoid dosimetric insufficiency.

Patient positioning and reproducibility	While the prone position has been shown to reduce small bowel volume in the pelvis, supine positioning is more reproducible and therefore preferred.[15,16] The use of knee and foot support is recommended, ideally indexed to the treatment couch. If the perineum is to be included the legs should be apart to minimise skin folds, using for example a vacuum bag or ankle stocks. Arms must be displaced out of the radiotherapy field; if para-aortic lymph nodes are to be treated, arms should be placed above the head and supported by a wing board or vacuum bag, for example. Attention should be given to bladder filling; while an empty bladder is more reproducible a moderately full bladder has bowel-sparing benefits.[17] All centres should follow a locally approved bladder-filling protocol specific for this patient group. An example drinking protocol may be: empty bladder, drink 350 ml in ten minutes, wait 45 minutes. The acquisition of two planning scans – one with an empty bladder and the second with a full bladder – has been advocated to model target motion and inform generation of an ITV or range of position for a LOP creation. Although a few studies discuss rectal preparation it has not been widely used in gynaecological radiotherapy.[18] Review of rectal volume on the planning CT is recommended and if anterior/posterior rectal diameter is >4–5 cm at the level of the target then a rescan with the addition of bowel preparation (eg, micro-enemas) should be considered. Centres should have a rectal management protocol in place for these situations.
Pretreatment imaging	IV contrast should be used (unless contraindicated) to aid delineation of pelvic lymph nodes. Acquisition of a planning MRI is advocated for primary cervix radiotherapy for which MRI/CT fusion aids target delineation and facilitates modelling of target motion. If a planning MRI is not available an empty bladder diagnostic MRI can allow evaluation of bladder-filling effects on target position. A PET/CT fusion can be useful for localising involved lymph nodes. If treating vaginal disease then a marker may be positioned at CT scanning to enable visualisation of the inferior extent of the tumour. A marker may also be placed to indicate the position of introitus. Some studies advocate the implantation of fiducial markers into the cervix or vaginal cuff to guide radiotherapy delivery.[19] This has predominantly been superseded by the use of volumetric verification imaging; however, it could be considered if centres are reliant on 2D imaging or if image quality is insufficient (eg, due to excessive bowel gas motion).

On-treatment verification	3D volumetric verification is the gold-standard imaging modality for this patient group, particularly if employing IMRT. Apart from primary cervix (intact uterus or uterine target), where daily imaging is strongly recommended as a minimum, images should be acquired for the first 3–5 fractions, systematic corrections applied (where suitable) and then repeated weekly. If 3D verification is not available or is limited then 2D imaging can be employed; however, this is not recommended when using IMRT. **Postoperative pelvis:** images should be registered to stable pelvic bony anatomy, bladder and rectal volume reviewed and the effect on target volume coverage assessed. Pelvic pitch rotations (tilt) can also affect target coverage and the application of systematic corrections in the anterior/posterior direction should be done with caution. When consistent deviations in pitch, bladder volume and rectal volume occur expert advice should be sought and where significant replanning considered. **Primary cervix (intact uterus or uterine target):** images should be registered to stable pelvic bony anatomy and online assessment of CTV coverage by the PTV contour performed. Assessment of rectal and bladder volume and pelvic pitch are also indicated. Set-up interventions should be made if the primary CTV is not adequately covered by the PTV contour and coverage can be improved through a simple mediation – for example, if CTV coverage can be improved by asking the patient to fill their bladder more (see example in Section 10.9, Appendix 14.5). To facilitate online review, centres are encouraged to educate radiographers to evaluate the relevant structures on cervical cancer volumetric verification images.[20,21] Implementation of prescriptive image review and decision-making protocols also aids uniformity of practice. Where para-aortic lymph nodes are being irradiated the treatment volume typically extends beyond the extent of standard CBCT parameters. In such cases extended verification images should be acquired and reviewed as a minimum weekly. **Vaginal RT:** bladder and rectal volume have a significant influence on vagina position and therefore 3D volumetric verification is the gold standard. **Vulva RT:** while 2D verification imaging is typically sufficient in this patient group, 3D should be used if available routinely or if using a highly conformal technique.

Site-specific issues

Bladder volume: uterus displacement is strongly related to changes in bladder volume, but its effect on cervix motion is less so.[8] The uterus can shift in the anterior/posterior or superior/inferior direction or rotate in the sagittal plane and lateral displacements are limited. Patients with relatively constant bladder volumes have less uterus movement, but bladder capacity and patient compliance are likely to change as treatment progresses.[1] See 10.9.1, Appendix 14.5 for examples of bladder volume variations affecting target coverage.

Rectal volume: rectal filling influences cervix and vaginal motion. Rectal volume changes cause anterior/posterior and superior/inferior movements of the CTV anatomy affecting both pre- and postoperative treatments. See 10.9.2, Appendix 14.5 for examples of rectal volume variations affecting target coverage.

Uterine distension: fluid can accumulate in the uterine cavity if natural drainage is compromised due to cervical stenosis. Cervical stenosis may be triggered by tumour invasion, inflammatory reaction or infection. In such situations the planned volume will likely not be sufficient to account for this distention and replanning necessitated. See 10.9.3, Appendix 14.5 for examples of uterine distention affecting target coverage.

Pelvic pitch: due to pelvic lymph node inclusion, treatment fields are long in the superior/inferior direction, so cervical cancer radiotherapy treatments are susceptible to rotational set-up variations. In particular, for patients with para-aortic irradiation, rotational errors can compromise target coverage.

Pelvic pitch can alter the position of the soft-tissue anatomy and the lumbar spine. L-spine position is important as the iliac lymph nodes follow the L5–L4 vertebra. Pitch is problematic as it cannot be corrected for with translational couch corrections and attempts to correct pitch at one part of the target can increase positional uncertainties at another point. If pitch set-up errors are consistent, extra caution must be taken when applying systematic corrections. See 10.9.4, Appendix 14.5 for examples of effect of pitch on target coverage.

Adaptive planning strategies in gynaecological cancer radiotherapy

To react to the changes seen in target and OAR positions now visible with online image guidance a number of different adaptive planning strategies are proposed in an attempt to further improve the accuracy of treatment delivery.

- **Offline replan:** deviations from planned delivery detected through IGRT protocols and assessed as leading to geographic miss of target or significant OAR displacement can be overcome through replanning. CTV-PTV margins may be adjusted to account for systematic OAR changes.

- **LOP:** at the planning stage a LOP is created based on variable bladder filling. After CBCT acquisition the most appropriate plan to account for daily anatomical changes can be chosen and delivered. This technique is now widely used for cervical cancer radiotherapy, leading to reductions in OAR doses.[1,22,23]

Future direction

The introduction of daily 3D IGRT improves the accuracy of treatment delivery and should be recommended for highly conformal techniques. To adapt to the observed changes in daily anatomy and residual errors to improve accuracy further requires the development of online replanning strategies (creating a new treatment plan based on the imaging each day). Due to the range of motion and variability observed in gynaecological cancer IGRT, these strategies are in development.

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10.10 Prostate

Background	The prostate is a mobile structure attached to the more mobile seminal vesicles, whose position can be dependent on the physiological motion of the rectum and bladder.[1] Pelvic bony anatomy is not an accurate surrogate for prostate gland position.[2] The failure to account for variations of the prostate position may compromise the biochemical control rate and can lead to increases in normal tissue toxicity.[3,4] Zelefsky *et al* demonstrated improved clinical outcomes with high-dose IGRT compared with non-IGRT for the treatment of clinically localised prostate cancer.[5] Toxicity after prostate and/or pelvic radiotherapy has reduced significantly with the iterative improvements in technique of conformal radiotherapy. The conventional or hypofractionated high-dose intensity modulated radiotherapy for prostate cancer (CHHiP) trial demonstrated that reduced margins translated into dosimetric benefits but not reduced side-effects, potentially because overall side-effect profiles were low with and without IGRT.[6,7] Hence further improvements in toxicity with the additional use of IGRT may be difficult to demonstrate.
Patient positioning and reproducibility	Patients should be scanned supine with knee and ankle supports improving prostate stability. We recommend providing patients with written guidance on the department's bowel and bladder protocols. **Bowel preparation:** bowel-emptying protocols should be in place. There is no robust evidence to recommend one rectal emptying strategy over another.[8] Options include mini-enemas, oral laxatives and dietary interventions. An empty bowel is more representative of treatment (rectal irritation will reduce its size after several fractions) and reduces the dose to the rectum, and therefore may decrease toxicity; this may also reduce rectum-induced intrafraction motion. Hydrogel spacers are stated to be an option by NICE but given the low risk of rectum toxicity may be more appropriate in strongly hypofractionated regimes. **Bladder preparation:** it is important to have a consistent bladder volume between planning and treatment. There are advantages and disadvantages of a full bladder.[9] A full bladder is associated with reducing dose to OAR, mainly the small bowel and bladder, but can be difficult to reproduce.[10,11] A bladder volume of 150 ml to 300 ml, if achievable, for pretreatment and treatment is recommended.[12] A bladder scanner has been used to help reduce repeat imaging but because of the limited impact of bladder filling on prostate motion (or bowel dose if minimum bladder filling is achieved) it has limited utility.[10]

Pretreatment imaging	For localised disease, scan from the bottom of the sacroiliac joints to the penile urethra (usually 1 cm below ischial tuberosities will be adequate). For nodal disease scan up to the L1/2 vertebral space. IV contrast is recommended when planning for pelvic nodal irradiation. Assess rectal volume prior to the full CT scan; if a rectal AP diameter >4 cm is seen, a repeat scan is recommended after voiding.[13] Fiducial markers (eg, gold seeds), if used, should be implanted approximately a week before planning to allow any periprostatic oedema to settle; fiducial migration is rare. In addition, a radiotherapy planning MR is desirable. This should be fused with the planning CT based on fiducial position where used or, if not, on anatomy of the prostate itself. MR-based delineation reduces target volume and improves knowledge of the dominant lesion allowing rational CTV margins (eg, prostate plus dominant lesion expanded by 4 mm).
On-treatment verification	The gold standard is to use daily online IGRT, matching to the prostate without action level. Margins could be reduced (with care) by using prostate IGRT, compared with bone match or tattoo alignment.[14] If daily prostate IGRT is not available, margins need to be increased, accepting a likely increase in toxicity. IGRT can be with fiducials or soft-tissue registration. Fiducials can be used for IGRT on planar kV and/or CBCT imaging. Daily online imaging with fiducials allows for all absolute translation errors to be corrected <1 mm. CBCT matching without fiducials has a higher inter-observer variability but does give volumetric information about deformation, SV and rectum position.[15] Prostate rotations can be large (up to 20 degrees) and so 6D correction is rarely beneficial. In addition, the round shape of the prostate makes rotation correction of limited utility and therefore 3D correction is appropriate and widely used. If lymph nodes are treated, correction for bone rotation has some benefit.[16] The main reason for poor visibility of the prostate on CBCT is mobile gas in the rectum and bowels creating reconstruction artefacts. Bowel control is therefore known to improve image quality.[17] Artificial metal hips can severely reduce CBCT image quality and such patients may benefit from verification using MVCT guidance. As the probability of prostate motion increases with time, for all IGRT strategies it is crucial to minimise time for imaging, time for decision-making prior to beam on and treatment time. If pelvic lymph nodes are also being treated, verification of the prostate gland should be the priority matching volume. For prostate bed irradiation soft-tissue matching is advised.

Site-specific issues	Intrafraction motion is known to range from 3 mm with short excursions as large as 2.2 cm. The effect of these geometric uncertainties in fractionated therapy, however, is small. The impact of intrafraction motion could be greater in hypofractionated regimes due to longer beam-on time and less averaging over fractions. It is therefore always important to be efficient but accurate when matching and to consider repeating verification imaging and correction mid-way during a fraction in ultra-hypofractionated regimes (eg, SBRT).

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10.11 Bladder

Background	3D volumetric imaging should be used because organ motion, mainly due to bladder filling, occurs independently to bony anatomy and can cause large variations in the shape and position of the bladder, leading to geographical miss. Furthermore, changes in rectal volume may lead to positional and deformational changes.[1,2] Inter- and intrafraction volume change can lead to shape changes rather than a three-dimensional vector displacement of a stable volume. A number of adaptive solutions have been suggested to compensate.[3,4] Currently the plan-of-the-day approach (see Section 7) is under evaluation in the RAIDER and HYBRID multicentre clinical trials.[5,6] Studies consistently show larger movements in the anterior and superior direction (up to 30 mm) and smaller movements laterally, inferiorly and posteriorly (requiring margins of about 10 mm).[1,2] This strongly argues for the use of anisotropic margins for internal organ motion, specifically those used in the RAIDER trial; 1.5 cm anteriorly and superiorly, 1.2 cm posteriorly and 0.8 cm laterally and inferiorly.[5]
Patient positioning and reproducibility	Patients should be supine in a comfortable and reproducible position to ensure stability. Immobilisation devices generally consist of a knee cushion and ankle support. A consistent bladder volume is important and whole-bladder treatments are delivered with an empty bladder. Patients should be counselled to avoid drinking fluids 30 minutes before and to empty their bladder immediately before the planning scan and each treatment. Catheterisation throughout planning and treatment in patients with a large residual bladder volume should be considered. Partial bladder or treatments boosting the tumour bed are generally delivered with a partially full bladder to improve normal tissue sparing.[3] The use of written patient information about bladder filling or emptying is strongly recommended. Attention should also be paid to rectal volume and enema and/or laxatives can be used to ensure more consistent rectal volumes.
Pretreatment imaging	CT with IV contrast should be used if treating the whole pelvis. Fiducial markers and cystoscopically inserted lipiodol can be used to identify the tumour bed and may be particularly helpful when using partial bladder radiotherapy or focal boost.[7] Multiple CT scans or PTV margins can be used to create an LOP (see Section 7).

On-treatment verification	Conventionally, relatively large population-based isotropic margins of 15–20 mm were applied to the CTV (whole bladder) to avoid geographical miss. This is a suboptimal approach for many patients because it can lead to excessive normal tissue being irradiated in those patients with smaller variations in position or conversely a geographical miss may occur in those patients with larger variations. As a minimum, CBCT should be used for the first three fractions to identify and correct for systematic errors (offline protocol). Online CBCT acquisition and verification is recommended to sufficiently visualise the bladder and rectum and reduce the risk of geographical miss due to internal organ motion. Up to 25 per cent of patients may have a systematic change in bladder size and/or shape and will require replanning.[2] In patients displaying significant random errors treated with smaller margins, partial bladder or boost techniques, daily online volumetric imaging is mandatory to reduce the risk of geographical miss. On acquiring CBCT a bone match should first be undertaken, bladder filling and PTV coverage then assessed and a correction made (or plan chosen in case of LOP) so that normal tissue irradiation is minimised. Ultrasound imaging can be used prior to CBCT to establish residual bladder volume.
Site-specific issues	Consider the nature of bladder filling and daily variability. The bladder is expected to move most in the anterior and superior directions. If CBCT images are uninterpretable because of rectal contents then remove the patient from the bed and ask them to try to go to the toilet and empty their bowels. Following this repeat CBCT and perform the match as described above. In the event that the bladder is full ask the patient to void again and repeat the CBCT. If the bladder remains full a member of the clinical team should be notified to ensure the patient is not in urinary retention. The patient's hydration may be different on chemotherapy days. Care should be taken when adjusting the drinking protocol (if used) on these fractions. Be mindful of minimising image match and correction time. If the bladder is consistently smaller then consider replanning.

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10.12 Sarcoma

Background	Soft-tissue sarcoma (STS) is a rare malignancy, accounting for approximately 1 per cent of solid tumours. Radiotherapy is used in the pre- or postoperative setting as part of a multi-modality treatment strategy for high-grade and selected low-grade tumours. Radiotherapy may be used as the primary treatment modality for inoperable tumours. This section comments primarily on extremity soft-tissue sarcomas. For extremity bone sarcomas, the same principles apply. For sarcomas of other body sites, such as the head and neck or thorax, we recommend immobilisation and imaging strategies described elsewhere in this document. Increasingly, IMRT and IGRT are becoming established techniques used in the treatment of extremity STS. Patients treated in the Radiation Therapy Oncology Group (RTOG) 0630 trial using IGRT had reduced late toxicity compared with a similar patient cohort treated without IGRT.[1] When using more conformal radiotherapy techniques, and with the greater use of preoperative radiotherapy, CBCT is required to verify limb position and to assess for tumour change. In the preoperative setting, changes in tumour volume are seen during treatment, which may have a detrimental effect on target dose coverage.[2–5]
Patient positioning and reproducibility	Due to freedom of movement and rotation in the limbs, effective immobilisation is a vital part of reducing patient positioning uncertainties. The ideal patient position is affected by factors such as beam entry positions, position of isocentre, avoiding unnecessary irradiation of the trunk or unaffected limb, preservation of a low-dose channel in the limb, patient comfort and stability. For arc therapy, and when using CBCT, it is necessary to ensure that the choice of patient position and isocentre does not lead to a collision between the gantry and the patient or couch. The build-up properties of materials need to be considered if beams enter through immobilisation equipment. Bolus will be required for some patients; the amount and position of bolus needs to be considered prior to making immobilisation equipment. There is a range of immobilisation solutions in practice, including combifix, thermoplastic shells, vacuum bags and in-house customisable devices.[6,7] Given the range of sarcoma presentations in both the upper and lower extremities and variable access to immobilisation equipment in different centres, it is unlikely that a single immobilisation technique will suit all patients.

	For lower limbs, it has been shown that immobilisation with a vacuum cradle, thermoplastic shell and indexing base plates results in quicker set-up times and a reduction in systematic error compared with a polystyrene vacuum cradle alone.[8] A simple immobilisation technique with indexed fixation points is likely to reduce the risk of daily set-up errors.
Pretreatment imaging	In the postoperative setting the surgical scar should be marked with wire. The joint above and below the tumour, the whole tumour bed and any surgical scars and drain sites should be included in the scan. The need for contrast at the time of simulation should be made on an individual patient basis and will depend on the site of the sarcoma and the OAR. Fusion of the planning CT scan with an MRI aids radiotherapy contouring in the preoperative setting. When possible, simulation MRI scanning should be performed in the treatment position using the intended MR-compatible radiotherapy immobilisation devices. Simulation CT fusion with a diagnostic MRI scan can be useful in aiding target volume contouring in the preoperative setting; fusion is less useful in the postoperative setting due to anatomical changes and is not recommended. Fusion with PET-CT scans may provide further information to aid delineation (eg, for Ewing's sarcoma). 4D CT may be of use when treating thoracic or upper abdominal sarcomas where respiratory motion is expected. Please refer to the advice regarding these techniques elsewhere in this document. The choice and position of markers will depend on body site and immobilisation technique used. Reference tattoos can be placed directly on the skin but also on thermoplastic immobilisation devices. In the postoperative setting, surgical clips may be identified on pretreatment and on-treatment imaging.
On-treatment verification	The frequency and on-treatment verification technique will be influenced by the equipment and resources available. kV, MV and CBCT are used in the UK. Imaging schedules vary from daily imaging to the first three days and weekly thereafter.[6] Daily online CBCT with correction will minimise positional errors with the most effective assessment of soft-tissue and bony anatomy but is more resource intensive and increases concomitant dose. Evidence from RTOG 0630 suggests that online daily IGRT is necessary to allow the use of reduced PTV margins.[9] This is supported by a case series of lower extremity STS patients treated with daily image-guided IMRT.[10] However, it may not be necessary for all patients to undergo this level of intense imaging and resources could be directed towards patients who have large displacements (>3 mm) during online image assessments.[11]

	Given the potential of the limbs to rotate, the effectiveness of immobilisation to minimise rotational displacements should be carefully assessed during imaging. Including the adjacent joint in the imaging FoV will facilitate assessment of rotation. There are limited data on the magnitude of rotations from the literature, but best practice suggests that individual patients should be set up again if imaging data reveal a rotation greater than three to five degrees.[10,12] If rotational stability is thought to be of concern, volumetric imaging modalities will be required to assess their true extent. However, a secondary analysis of the two most common imaging modalities used in the RTOG 0630 (kV orthogonal imaging and MV CT) suggests there was no difference in the magnitude of translational corrections between orthogonal and volumetric imaging. It should be noted that case series evidence suggests planar MV imaging requires larger CTV-PTV margins.[8] Compared with 2D imaging, CBCT provides a better assessment of contour change due to limb swelling or tumour growth or shrinkage. See the example in Section 10.12, Appendix 14.5. **Recommendations** Daily online imaging is necessary when using reduced margins (0.5 cm PTV). There is no evidence to suggest superiority of volumetric to orthogonal imaging when traditional margins are used. An assessment of rotations should be performed.
Site-specific issues	Alterations to limb contour can occur as a result of developing limb oedema, changes in a post-surgical seroma/haematoma or tumour shrinkage or growth in the preoperative setting. Reference tattoos and immobilisation should be reassessed for suitability throughout the duration of treatment. The dosimetric effect of limb changes should be assessed during treatment; if significant, a replan should be considered. For some upper limb tumours it may not be possible to perform orthogonal imaging due to the patient's body blocking the imaging beam; in this situation it may only be possible to image an anterior/posterior direction if CBCT is not available. Some STS treatment fields may be longer than the FoV of the imaging technique used.

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10.13 Lymphoma

Background	In recent years there has been a shift from anatomically-based involved-field radiotherapy techniques towards reductions in target volumes with involved-site radiotherapy (ISRT) based on the pre-chemotherapy disease extent, aiming to maintain treatment efficacy while minimising the sequelae of treatment.[1,2] Lymphoma may involve virtually any anatomical site in the body. Depending upon anatomical site, methods of motion management including 4D simulation or breath-holding techniques may be valuable to reduce volumes of irradiated normal tissues. Highly conformal treatment delivery using intensity-modulated radiotherapy is appropriate in some anatomical sites (particularly head and neck, mediastinum) to reduce treatment toxicity.[3,4] The method of image guidance depends upon anatomical site, method of treatment delivery (eg, opposed fields, conformal planning, IMRT) and visibility of the target volume on volumetric imaging. The site-specific guidance elsewhere in this document can be adopted for the majority of lymphoma cases. Some challenging lymphoma-specific scenarios are addressed in more detail.
Patient position and reproducibility	For neck treatment, an extended neck position may be adopted if this will facilitate sparing of adjacent regions (eg, oral cavity). Mouth bites may be appropriate for paranasal sinus treatment. For axilla and mediastinal treatments an arms-up (eg, using wing boards) or arms-down (eg, using a thermoplastic mask with five-point fixation) position can be adopted. Stomach treatment requires an arms-up position with a fast of at least two hours to ensure an empty organ. For pelvic treatment consideration needs to be given to whether to treat with bladder full or empty. Techniques for motion management (eg, breath-hold or 4D CT imaging) can be considered for sites affected by respiratory motion (lung, stomach, spleen). DIBH can be advantageous for some mediastinal treatments, in particular treatment of the superior mediastinum, where it allows a reduction in irradiation of normal lung and heart.[5,6] End exhale breath-hold can be used for treating stomach/spleen lymphoma although patient selection is more critical as this can be less well tolerated than DIBH.
Pretreatment imaging	Use of intravenous contrast is recommended for involved nodal sites. Oral small bowel contrast can aid delineation of mesenteric target volumes. For stomach treatment a small volume of oral contrast (eg, 50 ml) is recommended and additionally intravenous contrast can assist in delineation of perigastric lymph nodes.

	With regard to target delineation, diagnostic pre-chemotherapy PET-CT is required for ISRT for many types of lymphoma.[1,2,7] Registration of a pre-chemotherapy treatment position PET-CT to a planning CT is an ideal scenario although often not possible due to differences in scan set-up. Additional target volume margins are required depending upon the quality and position of pretreatment imaging along with anatomical changes.[1,2,8] For CNS lymphoma, registration of post-chemotherapy MRI with residual abnormality is valuable if additional dose is to be delivered.
On-treatment verification	Verification of lymphoma follows the principles detailed in the relevant site-specific guidance. When considering the method and frequency of verification it is important to consider the sources of error in the pretreatment process, the conformality of treatment planning and whether motion management has been adopted. In general, 3D conformal planning requires 2D imaging as a minimum with 3D imaging advisable with IMRT techniques. This section will focus on the more challenging areas, in particular the mediastinal and abdominal sites. **Mediastinal lymphoma:** there is a lack of evidence to guide optimal image verification of mediastinal radiotherapy with DIBH.[9] 3D imaging is appropriate in view of internal anatomical changes in DIBH (see the example in Section 10.13.1, Appendix 14.5). However, a cone-beam scan may require two to three breath-holds to complete, potentially requiring a manual start/stop with associated uncertainty. The requirement for daily verification will depend upon the reproducibility of DIBH/patient position. 3D imaging is recommended for the highly conformal 'butterfly' VMAT.[4,10] **Abdominal lymphoma:** the lack of soft-tissue contrast with CBCT makes verification of abdominal targets difficult. This is particularly challenging with the potential mobility of mesenteric targets; this uncertainty needs to be accounted for in PTV margins.[11] The use of CBCT versus bone matching with 2D verification may depend upon whether the target volume can be identified on CBCT. Daily CBCT should be considered for all cases. Sites such as the spleen and stomach, which have large CTVs, require volumetric imaging due to the proximity of OAR and the risk of organ motion in these sites (see the example in Section 10.13.2, Appendix 14.5). In addition to reducing motion of the organ, DIBH produces a better image quality due to the reduction in motion blurring (see the example in Section 10.13.3, Appendix 14.5).[5] If 4D CT is used for treatment planning, 4D CBCT verification may be used to assess potential motion issues.[12]

Site-specific issues	The acquisition of pre-chemotherapy PET-CT imaging in a radiotherapy treatment position (when at that stage of the diagnostic pathway many of these patients will not require radiotherapy) is very challenging to implement. The similarity of position of pretreatment imaging along with feasibility and accuracy of any registration to planning CT directly impact upon the clinical judgement of the required margin to generate a CTV.[1,2,8]

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10.14 Spinal metastases treatment with SABR

Background	In recent years the use of SABR for spinal metastases has increased, particularly in North America, where both choice of treatment technique and dose regime vary widely. Rates of vertebral compression fracture appear lower with multi-fraction treatment.[1,2,3] The surrounding normal tissues, in particular the spinal cord, must receive lower doses than the prescription dose, in order not to exceed the tolerance of these tissues.[4] To respect the tolerance of the spinal cord (or spinal cord OAR), some under-coverage of spinal SABR PTV by the prescription isodose is not uncommon.[4] It is recommended that precise patient immobilisation and intrafraction imaging (for long-duration treatments) is used to ensure the accuracy within the small PTV and OAR uncertainty margins required for SABR treatment. This must be combined with optimal pretreatment imaging using a multi-modality approach along with mandatory image guidance before every treatment delivery.[4,5] For longer treatment delivery times (eg, ten minutes or more), some form of intrafraction motion monitoring is recommended to maintain set-up errors to within 1–2 mm.
Patient positioning and reproducibility	Patients with tumours superior to T4/5 should be treated with a thermoplastic shell that immobilises the shoulders. Patients with tumours at T5 or inferior treated on a standard linear accelerator should be treated on an indexed wingboard or similar combined with a vacuum bag or body frame device to ensure that their arms are fully immobilised.
Pretreatment imaging	All patients should have a planning CT scan to cover the entire treatment area as well as any OAR for which dose-volume histograms are to be produced. Particular consideration should be paid to CT scanning limits for non-coplanar beam approaches where additional CT information is required to adequately define OAR doses away from the lesion(s). MR imaging should also be performed to reduce the target and organ delineation error component of the uncertainty margin.[5] MRI ideally should be performed in the treatment position to allow adequate image co-registration of the MRI scan with the planning CT scan prior to contouring. Unless deformable image registration has been adequately validated, rigid body registration should be used to co-register images. It is advised to MRI scan the vertebral body with disease plus a minimum of one vertebral body superior and inferior to disease and that a minimum of three vertebrae are used for image co-registration to planning CT. Matching the patient's physical spinal flexion between planning CT and MRI optimises the rigid image co-registration accuracy.

	Particular attention should be paid to this when imaging the cervical spine as small changes in position can bring about differential flexion between planning CT and MRI that cannot be accounted for in six-degrees-of-freedom rigid image co-registration. Contouring the spinal cord on MRI alone may be unreliable in the setting of patients with spinal instrumentation causing artefact (eg, in the setting of postoperative treatments) and here CT myelogram could provide additional useful information.[6] CT contrast should be used at the clinician's discretion. For lesions in the lower cervical or upper thoracic spine, contrast may assist with the delineation of the brachial plexus.
On-treatment verification	It is essential that treatment delivery is guided by online imaging, which for linac-based approaches is optionally performed on a machine with a couch capable of six-degrees-of-freedom correction. Repeat imaging should be considered after correction and following treatment delivery to quantify intrafraction motion. For longer treatment times (for example, when using CyberKnife or when using planar X-ray-based image guidance), consideration should be given to intrafraction imaging to ensure accuracy of treatment delivery, as discussed above. See Section 10.14, Appendix 14.5 for imaging examples.
Site-specific issues	**Expected problems and changes with treatment for each site:** an MDT approach should be taken to troubleshooting, involving clinician, physicist and radiographer. If CBCT is used for treatment imaging, OAR tolerance isodose structures may be useful to aid MDT discussions on matching priorities. **External contour change:** weight gain or loss can result in dose being reduced or increased. SABR techniques will mostly use an unflattened (soft) beam and treatment is delivered over a small number of fractions, meaning that any change in patient contour is more significant and more time-critical than for patients receiving conventionally fractionated radiotherapy. Where CBCT is used, centres should have clear protocols indicating patient external contour change checks and tolerances. Although VMAT delivery is less susceptible to patient contour change than fixed-field IMRT, contour changes >0.5 cm from the planning CT should be investigated dosimetrically on a patient-by-patient basis as relatively small external changes can have an impact on the dose at the isocentre.

On-treatment image quality: where visualisation of relevant anatomy is difficult, optimisation of image acquisition settings should be considered (eg, a higher dose imaging preset may be created). This can be decided after the fraction one image has been reviewed.

Patient rotation: due to the location of the target volume and spinal cord, efforts should be taken to minimise rotation. A robotic couch able to correct in six degrees of freedom is highly recommended for linac-based treatments. Efforts should be taken to minimise rotations, ensuring that patients are repositioned if the rotational values exceed the correctional range of the robotic couch. If no robotic couch is in use, rotations should be kept low enough to ensure that any uncorrected patient rotation leads to translational set-up errors that are well within the set-up margin. This must be assessed on a case-by-case basis at each treatment.

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10.15 Palliative

Background	Palliative radiotherapy accounts for approximately half of all radiotherapy treatment courses.[1] External-beam palliative radiotherapy is delivered for a range of indications and can be delivered to any anatomical site in the body. The planning technique used for palliative treatment is influenced by the patient's symptoms, the need to provide swift or emergency treatment, the patient's performance status and prognosis and departmental resources. Simple planning techniques are delivered with wider margins to field edge often in keeping with the margins dictated by 2D online imaging techniques.[2] Conversely, patients planned with conformal techniques, including IMRT or VMAT, are often planned with smaller margins reflecting the planning and subsequent online imaging processes employed. Planning the treatment and using online imaging may reduce dose to normal tissues; however, the clinical benefit of this has not been demonstrated in palliative radiotherapy.[2] In the palliative patient population, the time required for planning must be weighed up against the expeditious delivery of a less complex treatment that may be quicker to start and deliver. Wide variation in palliative treatments is recognised. Careful case selection may support delivery of more complex treatments to patients with a better prognosis for whom durability of symptom control is required.[3] This guidance applies to simple planning techniques and specifically excludes highly conformal and IMRT planned treatments, which are addressed elsewhere.
Patient positioning and reproducibility	To ensure reproducible treatment set-up, patient comfort must be taken into consideration. In conformally planned fractionated treatments, set-up will reflect that of a radical treatment course to the same anatomical site. Treatment set-up and image guidance should reflect the delivery technique, the need for a reproducible position and, importantly, the patient's comfort. Additional immobilisation devices may be beneficial, such as knee blocks for reproducibility and a mattress or other cushioning to aid comfort. Beam-directional shells may also be required for treatments to the brain, base of skull and upper C-spine if lateral fields are used. While standardised set-up guidelines can be helpful, flexibility is required given the nature of the treated population.

Pretreatment imaging	Referral for palliative radiotherapy planning should detail the specific site to be treated, alongside any necessary information regarding the need for clinical mark-up. While craniocaudal limits for most palliative planning scans will be carried out in line with local protocols, those for spinal and long-bone metastases, alongside skin lesions, may require more detailed information from the referrer. The planning scan limits should reflect the treatment site, allowing generation of a DRR to support online image matching. For spinal treatments it may be necessary to extend the imaged field beyond the normal range to ensure certainty of the spinal level to be treated. Increased scan length may also be required when multiple sites are to be treated. CT virtual simulation may be quicker than conventional screening simulation and therefore reduce the time the patient has to lie in the treatment position for image acquisition. There is some limited evidence that CT simulation may help to reduce field sizes and thereby the dose to normal tissues.[2] The impact on clinical outcomes is, however, unclear. Traditional screening simulators are being phased out across the UK and CT simulation should be considered the gold standard. The use of screening simulators can only be justified where skill sets are available and then only where bony landmarks can be used to define the field. Reference tattoos/marks for localisation are commonly required and should be sited according to the site treated. Oral/IV contrast is rarely required in palliative radiotherapy but may be considered where essential to aid delineation. Likewise, multi-modality imaging is typically only required for diagnostic purposes. For conformally planned treatments, where breathing motion can influence planning, a 4D CT may be justified.
On-treatment verification	The benefit of imaging to detect random errors and systematic set-up errors is as important as it is with radically planned patients. Online imaging should be considered the gold standard. Given the short duration of most palliative treatments, the use of offline image review, with the resultant delay to correction, is unlikely to be appropriate. Online imaging for the detection of gross error is essential before the first treatment fraction is delivered, including where a single fraction is used. The use of online daily imaging for fractionated treatments can be considered where a systematic set-up error correction cannot be achieved.

	Orthogonal 2D kV or 2D MV imaging for a bony anatomy match can be used. Online images must be large enough to include bony landmarks to allow matching. Care should be taken when matching to structures away from the treatment isocentre and treatment volume as this may give unreliable results. Cone-beam CT may be appropriate: ▪ For isocentrically planned treatments ▪ Where MV/kV 2D images are not sufficient to perform an anatomical match ▪ Where changes to internal anatomy are likely to impact on the effectiveness of treatment ▪ In departments that do not have a lot of experience with 2D imaging. MV interrupt imaging using the treatment fields should be considered only if there is sufficient visible anatomy to accurately perform an image match.
Site-specific issues	Departments should optimise the quality of the reference DRR for 2D verification. Acceptable tolerances and action levels are likely to be influenced by the frail condition of many patients undergoing palliative radiotherapy.

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11. Abbreviations

2D	Two-dimensional
3D	Three-dimensional
4D	Four-dimensional
AIP	Average-intensity projection
ALARP	As low as reasonably practicable
ART	Adaptive radiotherapy
BIR	British Institute of Radiology
CBCT	Cone-beam CT
CECT	Contrast-enhanced CT
cGy	Centigray
CNS	Central nervous system
CT	Computed tomography
CTV	Clinical target volume
DCR	Digitally composited radiographs
DIBH	Deep-inspiration breath-hold
DICOM	Digital Imaging and Communications in Medicine
DIR	Deformable image registration
DRR	Digitally reconstructed radiographs
DVH	Dose-volume histogram
EPI	Electronic portal imaging
ESTRO	European Society for Radiotherapy and Oncology
EUS	Endoscopic ultrasound
FB	Free breathing
FDG	Fluorodeoxyglucose
FoV	Field of view
GTV	Gross tumour volume
Gy	Gray
IGRT	Image-guided radiotherapy
IPEM	Institute of Physics and Engineering in Medicine
IMRT	Intensity-modulated radiotherapy
IR(ME)R	Ionising Radiation (Medical Exposure) Regulations
ISRT	Involved-site radiotherapy
ITV	Internal target volume
IV	Intravenous
kV	kiloVoltage

LOP	Library of plan
MDT	Multidisciplinary team
MIP	Maximum intensity projection
MLC	Multi-leaf collimator
MRI	Magnetic resonance imaging
MPE	Medical physics expert
MV	Megavoltage
NCAT	National Cancer Action Team
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRAG	National Radiotherapy Advisory Group
OAR	Organ(s) at risk
ODN	Operational delivery network
PACS	Picture archiving and communication system
PET	Positron emission tomography
PHE	Public Health England
PRV	Planning risk volume
PTV	Planning target volume
QA	Quality assurance
R&V	Record and verify
RCR	The Royal College of Radiologists
ROI	Region of interest
RMS	Root mean square
RTOG	Radiation Therapy Oncology Group
SABR	Stereotactic ablative radiotherapy
SCoR	Society and College of Radiographers
SD	Standard deviation
SE	Standard error
SGRT	Surface-guided radiation therapy
SRS	Stereotactic radiosurgery
STS	Soft-tissue sarcoma
SV	Seminal vesicle
TPS	Treatment planning system
UK	United Kingdom
VMAT	Volumetric modulated arc therapy

12. Glossary

Action level	An action level for a measurement or parameter may be defined as the point at which further action is necessary.
Adaptive radiotherapy	Refers to the alteration of the radiotherapy treatment plan to compensate for changes in both tumour and normal tissue anatomy.
Clinical target volume	A clinically defined target volume that contains the demonstrable tumour (gross tumour volume) unless it has been surgically excised and microscopic invisible tumour. This volume contains cancer cells and must be treated with the prescribed radiation dose adequately to achieve a cure.
Concomitant exposure	Any exposure within the course of the radiotherapy process that is not a treatment exposure.
Cone-beam computed tomography	A medical imaging technique consisting of X-ray computed tomography where the X-rays are divergent, forming a cone. The X-ray images are reconstructed into a 3D volume to allow volumetric imaging on the treatment machine.
Conformal radiotherapy	A treatment technique that aims to shape the 3D high-dose volume to the PTV while minimising dose to healthy tissue.
Critical structures	Normal tissues or organs near the tumour whose tolerance dose for serious late radiation damage limits the amount of radiation that can be administered.
CT simulator	A specially designed CT scanner with a flat-top couch and a laser field positioning system. It can provide 3D CT images for tumour volume localisation and can also reconstruct an equivalent simulator radiograph, thus providing virtual simulation. In addition, 4D CT simulation can be used to acquire images to capture motion and allow more accurate outlining of moving targets and the generation of patient-specific margins.
Digitally composited radiograph	Similar (geometrically) in construction to the digitally reconstructed radiograph, but uses selective suppression or enhancement of various ranges of CT numbers that relate to certain tissue types.
Digitally reconstructed radiograph	A planar radiograph made by computer-projected rays through 3D CT density information.
Displacement (or deviation)	The difference in a measured parameter from its reference value. It may be positive or negative.

Dosimetric verification	The process of assessing the correctness of the delivered dose to the patient with respect to the desired reference, defined by the treatment plan. The procedure is termed *in vivo* dosimetry when it is performed on the patient during a treatment fraction.
Fiducial (marker)	An object placed in the FoV of an imaging system that appears in the image produced, for use as a point of reference or a measure. It may be something placed either on or in the patient and is used as surrogate for the tumour position for IGRT.
Gating (respiratory gating)	A delivery technique that allows the treatment of tumours at certain defined points in the respiratory cycle.
Geometric error	A systematic error introduced during the imaging process, due either to imaging hardware (eg, misaligned CT lasers) or inherent geometrical inaccuracy of the imaging modality (eg, MRI). Contributes to the phantom transfer error.
Geometric (treatment) verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan.
Gross errors	Geometric displacements in patient set-up (localisation) with respect to the desired reference defined by the treatment plan, which are deemed to be of such a magnitude that the set-up *must* be changed, either during the current fraction or in the following fraction. Any particular treatment technique will have a normal distribution of random set-up errors for the patient population. A set-up error may be considered to be gross if its magnitude is greater than 1 cm or 3 × SD of the population data, whichever is the smaller.
Image acquisition	The process of acquiring image data. In the context of geometric verification, it may be a 2D (planar) or a 3D (volume) set of data, and may be obtained with either ionising or non-ionising radiation.
Image registration	Methods of aligning two 2D or 3D image sets (eg, CT, MRI, PET). Image sets may be overlaid or structures may be mapped between the sets.
Imaging protocols	A set of procedures, instructions and processes put in place to acquire, analyse and store images for the purpose of (in this context) geometric treatment verification.
Immobilisation	A set of instructions, processes and/or equipment used in conjunction with the patient to ensure accurate and reproducible geometric set-up both during a single fraction and from one fraction to the next. The same immobilisation should be used at all points in the radiotherapy process.

Interfractional verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan, from one fraction to the next.
Intrafractional motion	Patient movement (which may be physical or internal organ motion) that may be present during a single treatment fraction. The movement may occur during delivery of a single exposure or at any time from the end of patient set-up through to the end of delivery of the final exposure for that fraction.
Intrafractional verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan, during a single treatment fraction. It may be assessed during delivery of a single field and/or throughout the period from the end of patient set-up to the end of delivery of the final exposure for that fraction.
Isocentre	A single point within the treatment room (in space) towards which the radiation beam always points. The central beam axis passes through this point, and on a linac the three principal rotational movements of gantry, collimator and floor are all around axes that intersect at this point. For a tomotherapy machine, it is a point of intersection between the centre of the scan plane and the axis of rotation of the scan circle.
Linac geometry error	A systematic error due to inaccuracy in the position of the radiation treatment beam from a chain of uncertainty in the linear accelerator. Examples are errors in the field-edge position, the focus skin distance indication or the isocentre location. It contributes to the phantom transfer error.
MR simulator	An MRI scan with a flat patient-indexed table that provides near identical patient positioning to CT simulation and can be used for contouring and treatment planning.
Offline treatment verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan, after the delivery of a treatment field and/or whole fraction. Desired geometric changes in patient set-up as a consequence of this process are conducted retrospectively in the following fraction(s).
Online treatment verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan, immediately prior to the delivery of a treatment field and/or whole fraction. Desired geometric changes in patient set-up as a consequence of this process are conducted prospectively during the fraction.
Orthogonal PAIRED images	A pair of 2D images (planar) acquired at 90 degrees gantry rotation to one another.

Patient set-up error	Any geometric displacement in patient set-up (localisation) with respect to the desired reference defined by the treatment plan that is due to the patient (eg, organ motion, respiratory motion, involuntary movement).
PET-CT simulation	Integrated PET with a specially designed CT scanner in a single unit with a flat-top couch and a laser field positioning system.
Phantom transfer error	The geometric displacement accumulated throughout the radiotherapy process (from pretreatment imaging through to treatment delivery). Comprises the geometric imaging error, the TPS error and the linac geometry error.
Portal imaging	Imaging of the part of the body being irradiated to check the accuracy of geometry of treatment delivery and sometimes also to check dosimetry.
Pretreatment verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan before the commencement of a course of radiotherapy.
Quality assurance	All procedures that ensure consistency of the medical prescription and safe delivery of that prescription with regard to dose to the target volume, together with minimal dose to normal tissue, minimal exposure to personnel and adequate patient monitoring aimed at determining the end result of treatment.[1]
Random errors	Geometric displacements in patient set-up (localisation) with respect to the desired reference defined by the treatment plan, which vary in both magnitude and direction for each treatment fraction. These are primarily due to variations of daily positioning and/or organ motion.
Real-time treatment verification	The process of assessing the correctness of patient set-up (localisation) with respect to the desired reference defined by the treatment plan in real time, during the delivery of a treatment field and/or whole fraction.
Record and verify system	Hardware and software designed to record and verify treatment parameters during a patient's treatment simulation and delivery. The system may contain software that can provide an electronic patient record and general database functions as well.

1. World Health Organization. Quality assurance in radiotherapy. A guide prepared following a workshop held at Schloss Reisenburg, Federal Republic of Germany, 3–7 December 1984.

Reference data set (images)	A 2D planar image or 3D volume image data set that represents the desired reference positioning of the patient's anatomy (the treatment plan) with respect to a datum. The datum may be an indication of the beam central axis or field edges (2D) or the isocentre (3D) of the treatment machine.
Registration (registration algorithms)	A means of comparing geometrically the anatomical position within one image with the same anatomical features within another, with respect to a datum. For the case of treatment verification, one image will be termed a reference derived from the correct desired isocentre position in the treatment plan and one will be an image acquired during the course of treatment. The images may be 2D planar images or 3D volume data sets. The datum may be an indication of the beam central axis or field edges (2D) or the isocentre (3D) of the treatment machine. The registration algorithm is the mathematical method used to perform the comparison.
Residual error	Displacement from the planned position remaining after initial correction has been made.
Set-up errors (field placement errors)	Any geometric displacement in patient set-up (localisation) with respect to the desired reference defined by the treatment plan that is present at the time of patient set-up during treatment delivery.
Systematic errors	Geometric displacements in patient set-up (localisation) with respect to the desired reference defined by the treatment plan that are similar in both magnitude and direction for each treatment fraction. These are primarily due to systematic differences in equipment or protocol throughout the radiotherapy process (that is, from pretreatment imaging to treatment planning to pretreatment verification, etc).
Target delineation error	The systematic error introduced and 'frozen' into the treatment preparation process at the time of target delineation. It represents the difference between the defined and 'ideal' CTV. Because this 'ideal' or standard CTV is not known, assessment of this error must be undertaken on a population basis using different methods. One approach to define a standard CTV may be the consensus CTV outline from a group of doctors working to the same protocol (inter-clinician). Another may be the mean CTV outline of a given target drawn repeatedly over time by the same doctor (intra-clinician). Once the standard or 'ideal' CTV is determined and the discrepancy evaluated, the target delineation error may be defined as the SD for this discrepancy. It is impractical to calculate this error on an individual patient basis and, as it cannot be quantified and corrected using imaging, the consequences of the target delineation error must be incorporated into the CTV-PTV margin.

Tolerance	The permitted observed variation in a parameter or measurement from its desired value.
Tomotherapy	A modality of radiotherapy that combines a linear accelerator, binary MLC and megavoltage CT scanner on a rotating gantry. IMRT is delivered in a continuous, helical (360 degree) fashion as the patient is moved through the rotating gantry on the couch.
Tracking	A form of monitoring, localising and following the tumour in real time during the radiotherapy treatment.
Treatment planning system	The hardware and software used for simulating the irradiation geometry to be used for patient treatment and for calculating the distribution of dose within the patient. Software tools use 3D patient data from CT and other imaging modalities to visualise volumes of interest. The main function is to design the optimum dose distribution with the patient in three dimensions. It can network with the linear accelerator and CT scanner and with facilities for designing shielding blocks and compensators.
Treatment planning system error	The systematic error resulting from either the treatment planning software or the interaction of that software with the rest of the treatment planning process. Contributes to the phantom transfer error.
Verification (geometric) protocols	A set of procedures, instructions and processes put in place to ensure the geometric correctness of the positioning of all patient set-ups (localisation) with respect to the desired reference defined by the treatment plan.
Volumetric modulated arc therapy	A type of IMRT in which the linear accelerator rotates around the patient during treatment. The machine continuously reshapes and changes the intensity of the radiation beam as it moves around the body.

13. Acknowledgements

13.1 Steering group

Preparation of this guidance has been led by a steering group with the following members:

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13.2 Working group

The guidance has been prepared by a large working group without whose help this would not have been possible. The steering group would like to thank the following for their input and contributions.

Megan Aldus
Marianne Aznar
Angela Baker
Colin Baker
Rachael Barton
Alison Blower
Claire Blowfield
Amy Bray
Kerrie-Anne Calder
Sophie Cattani
Guy Chetiyawardana
Ananya Choudhury
Zankhana Jani
Kirstie Johnson
Mike Kirby
Sri Kumar
Narinder Lalli
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Steven Landeg
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Richard Garratt
Rebecca Goody
Shaista Hafeez
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Victoria Hammond-Turner
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Paul Hatfield
Stephen Hedley
Robert Huddart
Alcia Morris
Rebecca Muirhead
Louise Murray
Mitchell Naisbit
Ros Perry
Kelly Picken
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Yvonne Rimmer
Christopher Scrase
Claire Sealby
Amy Shaw
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Helen Turnbull
Louise Turtle
Bronwyn van Blerk
Mark Warren
Amy Wilson
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14. Appendices

Appendix 14.1. Derivation of systematic and random errors, and relationship to the CTV–PTV margin – offline protocols

The following guidance for offline protocols is based on *On target: ensuring geometric accuracy in radiotherapy*, a joint document from The Royal College of Radiologists, Society and College of Radiographers and Institute of Physics and Engineering in Medicine published in 2008 and now withdrawn.

Although not included in the main body of the new guidance, we have added this as an Appendix to *On Target 2: updated guidance for image-guided radiotherapy* as offline protocols are still in use in some centres. Offline protocols are now much less commonly used as most centres have automated couch correction and tend to correct for all errors.

Corrective strategies

The key requirement in any imaging protocol, apart from gross error detection, is to provide an accurate estimate of systematic set-up error. Depending on action level, the chosen correction strategy can then be used to remove this error. The protocol must confirm any applied correction is valid and remains so for the duration of the treatment.

Figure A1 shows the effect of a poor correction strategy. The blue triangles indicate the set-up error measured from a portal image. The red line indicates the systematic set-up error (SSE), calculated as the average displacement over four days. For this patient, the SSE has been determined as being the largest (or last) value seen over the four days and a correction applied to that value. This method is repeated for the next four sets of images. The result is an exaggerated oscillation in the accuracy of the patient set-up. Figure A2 shows the outcome on set-up if the SSE had been correctly calculated and actioned.

Assessment and correction of systematic errors

It is important to assess the SSE accurately within an appropriate number of fractions so that (a) a robust estimate of the true systematic error can be made, while (b) the minimum number of fractions is delivered with the systematic error present.

Two possible approaches are the no action level (NAL) and shrinking action level (SAL) correction strategies.

- The NAL is most commonly advocated for radical treatments.[1,2] It involves the systematic error being calculated after 3–4 fractions and a correction performed that is the total magnitude of the systematic error, regardless of the tolerance for that treatment site. Since the NAL approach does not define an action level for corrections, there is also a sub-population of patients in whom the systematic error is so small that applying a correction would be impractical; for example, moving the couch <2 mm. It is suggested that only systematic errors of >2 mm should be corrected. The extended NAL protocol (eNAL) includes once-weekly imaging in addition to imaging in the first 3–4 fractions. If the result is within tolerance there is no action. If out of tolerance, further images are obtained to determine systematic error. This is useful in detecting trends and systematic changes to the patient's set-up over the treatment course.[3] The NAL protocol does not act on gross errors. Such errors should be corrected before a further fraction is given.
- The SAL uses an action level that reduces according to the number of fractions imaged.[4] The running mean error over all acquired images is compared with the current action level and treatment set-up adjusted by this amount if the discrepancy exceeds the action level. The final action level is determined by the initial action level and number of images considered appropriate for the particular technique. The SAL avoids a set-up

being corrected prematurely, where discrepancies observed at the start of treatment may have arisen through random rather than systematic error. A disadvantage of the SAL is that following any correction the process is restarted and information obtained prior to the restart is lost.[5]

Figure A1. Effect on set-up of poor correction strategy

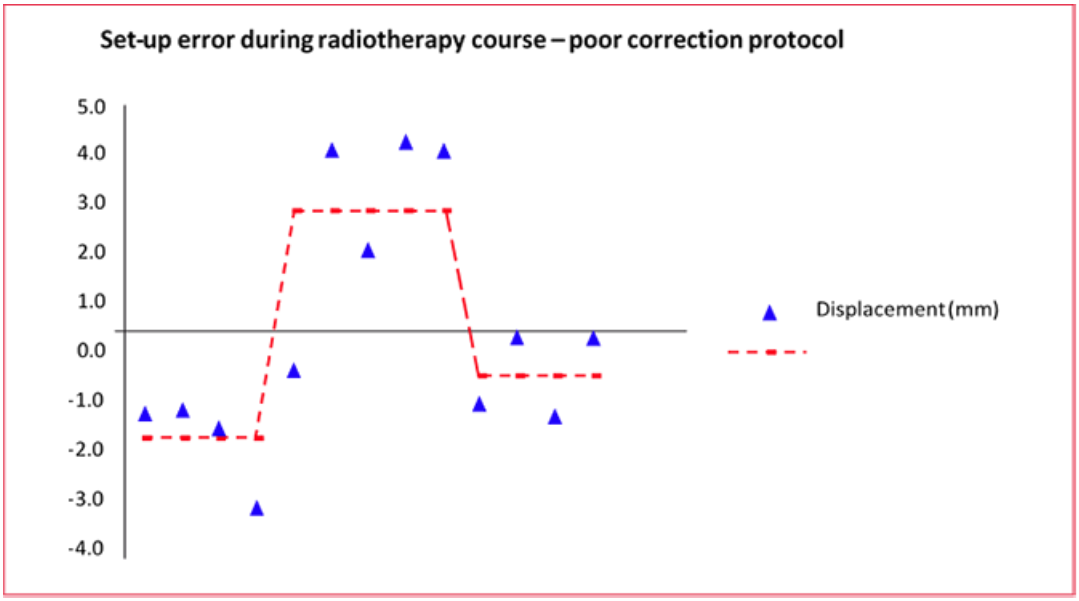

Figure A2. Outcome on set-up if the SSE is correctly calculated and actioned

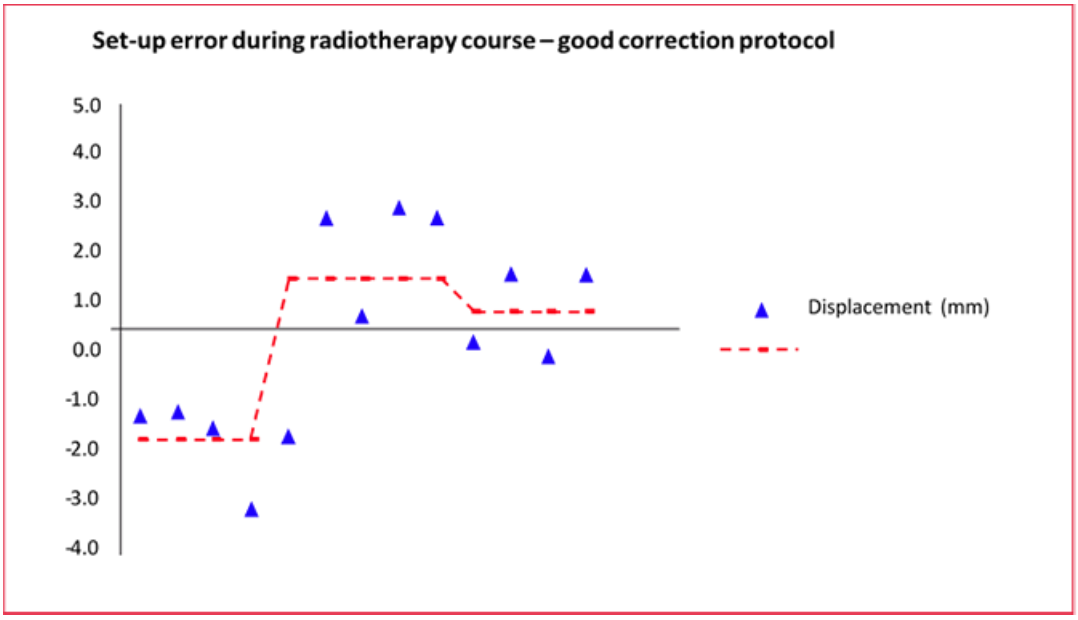

Figure A3. Changes in set-up depicted during a fractionated course of radiotherapy to illustrate the concepts of gross error, tolerance and action levels using a NAL protocol (read left to right, top to bottom)

A direct comparison of the SAL and the NAL protocol using an average of ten imaged fractions per patient found the NAL protocol to be more efficient in terms of number of images per reduction in systematic error.[2]

Figure A3 illustrates the difference between tolerance and action level using a NAL protocol.

Summary of offline corrective strategies

- A NAL strategy will correct the systematic component of the set-up error after at least three fractions.
- A SAL strategy uses an action level that decreases according to the number of fractions imaged, in order to remove the systematic component of the set-up error. Workload may increase as a consequence.
- All corrections applied to the treatment set-up must be verified.
- Weekly imaging is recommended in addition to the correction policy.

Example of control of systematic components

For a given treatment population, it is decided to implement a protocol designed to correct mean set-up errors greater than 2 mm. For an uncorrected patient group, a portal imaging study for this population reveals a systematic set-up error ($\sum_{set\text{-}up}$) of 3 mm. Application of an off-line correction strategy has the effect of reducing the accumulated contributions of both the patient set-up and the phantom transfer error (see Section 14.1) It has been shown that correcting the mean set-up over the course of treatment to within ±X of the expected position gives a theoretical approximation to this combined SD of X/√3.[6] This corresponds to 1.2 mm for the example of X=2 mm. Table A1 gives representative values for the contributing systematic components for a prostate treatment and shows the combined systematic error for the uncorrected and corrected cases.[7]

Table A1. The effect of an off-line correction strategy on the systematic components of the CTV-PTV margin

Systematic errors (mm)	No correction	Correction
$\sum_{delineation}$	2	2
$\sum_{motion}$	3	3
$\sum_{transfer}$	3	Combined error = 2/√3 = 1.2
$\sum_{patient\ set\text{-}up}$	3	
∑ (sum in quadrature, see Equation 7)	**5.6**	**3.8**

There is, therefore, a reduction from 5.6 to 3.8 mm in the combined systematic set-up error as a result of employing a correction protocol. For a typical margin recipe, the constant '**a**' has a value of 2.5 leading to a theoretical margin reduction of 2.5 x 1.8 = 4.5 mm for this example.[8,9]

Following full implementation of the correction protocol, a portal imaging study repeated on the corrected patient group data should give a theoretical value closer to $\sum_{set\text{-}up}$ = 1.2 mm.

This example demonstrates how a correction strategy designed to limit the mean set-up error constrains the combined effects of ∑patient set-up and ∑transfer and can lead to a reduction in the calculated CTV-PTV margin.

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Appendix 14.2. Illustrative example of the change management framework

Scenario: 4D CBCT has become available in a department due to a machine upgrade – what happens now?

The worked example on the following pages is for illustrative purposes only and should not be applied verbatim in any particular centre. Individual centres should perform their own analysis, in particular of the risks.

Project stage 1: define the goals

Identify project leads

- Form MDT to discuss the role/potential of 4D CBCT in the department.
- Ensure there is a clear understanding of both the function of the technology and also any relevant terminology.
  - What is 4D CBCT, what are its advantages and drawbacks?

Why is the change necessary?

- Define the clinical motivation to implement 4D CBCT.
  - What treatment technique(s) could benefit and how?
- Is there a valid (easier/less demanding) alternative? For example:
  - 4D CBCT is not required for gated treatments as treatment can be verified by standard CBCT.
  - 4D CBCT is suitable for patients with an ITV to assess the range of motion.
- Set up an MDT approach and regular meetings.
- Undertake a comprehensive review of current literature regarding clinical motivation for using 4D CBCT.
- Understand department requirements and all elements of the treatment pathway.
- Discuss with other departments to get a feel for availability, uptake and use of 4D CBCT both nationally and internationally.
- Evaluate the number of linacs with 4D CBCT capabilities and the potential patient numbers who would benefit from this technique (for example, those where the tumour motion amplitude exceeds 1 cm).[1]

Project stage 2: establish the baseline

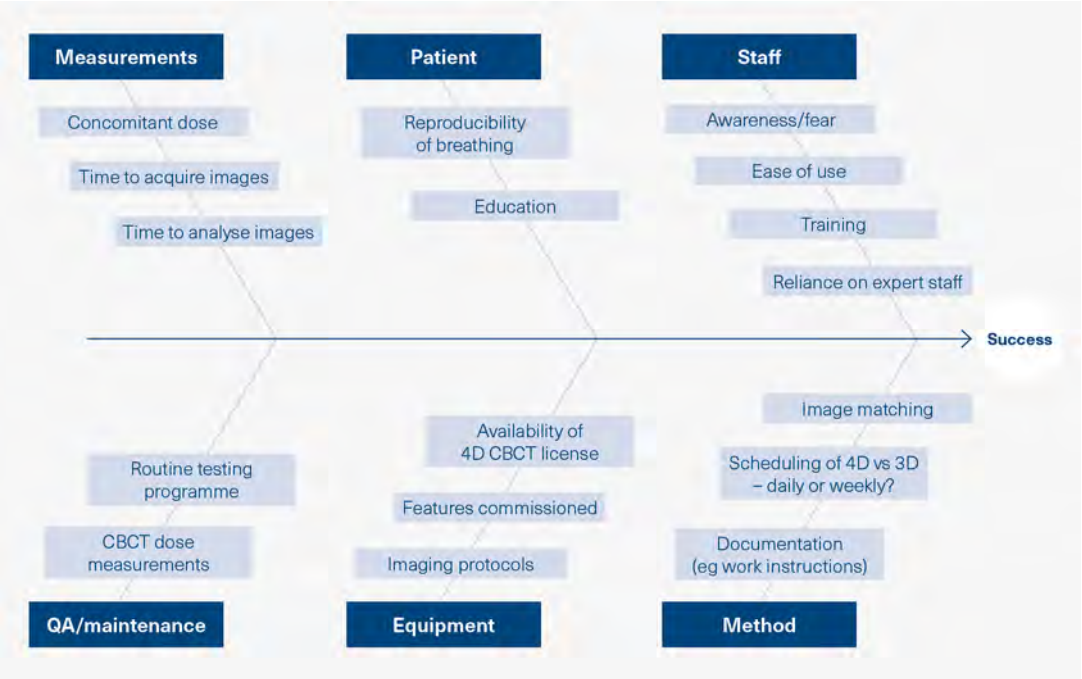
Description of the current state

- How many patients cannot be set up properly because the tumour is poorly visible in 3D CBCT, and who are these patients?
- Consider the entire treatment pathway. For example, imaging at treatment is linked to the demands of the treatment planning process.
- 4D CBCT may mostly be of benefit/appropriate when 4D CT is used for treatment planning.
- 4D CBCT is not applicable with the use of DIBH, end-expiration breath-hold (EEBH) or gated treatments.
- Does the need to use 4D CBCT depend on the use of abdominal compression devices?

Limiting factors

Identify factors that inhibit change. For example, lack of capable machines (see Figure A4).

Figure A4. Ishikawa Diagram demonstrating the key factors for the planned implementation of online 4D CBCT[2,3]



Project stage 3: design and prepare

Risk assessment and mitigation of risks

- 4D CBCT may be associated with an additional imaging dose to the patient in comparison with 3D CBCT.
  - Justification will be required by the IR(ME)R practitioner.
- Is 4D CBCT inferior/equivalent/superior to current practice?
  - Inferior – do not implement.
  - Equivalent – may not be worth implementing.
  - Superior – consider implementing.

Where there are benefits in some aspects and not in others, 4D CBCT needs to be tailored to the most clinically appropriate scenarios to make the time, dose and effort beneficial to the patient (see Table A1).

Preparation of actions

- Propose pilot project on a small number of cases (for example, five selected free-breathing, non-gated lung patients).
- Create a 4D CBCT protocol for acquiring 4D CBCT.

Regular review of actions

- Keep tempo by regular review of actions.

Project stage 4: test and refine prior to full implementation

End-to-end tests

- Use motion phantom – CT for planning and CBCT for verification.

Pilot project

- Train key team members in the use of 4D CBCT.
  - Manufacturer training should be undertaken to ensure safe and efficient use of technology by department engineers, physicists and radiographers.
  - A new competency package should be developed by the MDT (this could be carried out in conjunction with a department where 4D CBCT is already in clinical use).
- Assess feedback from team members who have undergone initial training to establish if the training package is suitable.
- Undertake end-to-end tests, in clinical mode, to ensure the team is familiar and confident with the new technology and processes.
- Select patients and images as for the 4D CBCT protocol (for example, 4D CBCT acquired the first fraction and weekly thereafter with 3D CBCT at all other fractions). 4D CBCT should be reviewed offline by the MDT.

Review of pilot and preparation of final project documentation

- Once the pilot project has completed, get feedback from users of 4D CBCT.
- Assess all images acquired during the pilot phase and critically evaluate the benefits and drawbacks of 4D CBCT, including quality of images, patient experience, length of treatment slots, dose and accuracy of treatment. Create action levels based on the information seen on 4D CBCTs from the pilot.
- Send the pilot results and feedback to the MDT for discussion. The impact of change, mainly dose and time, needs to be addressed and any troubleshooting measures and learning from the pilot need to be put in place.

Project stage 5: full implementation and review

Project go-live

- Once clinical implementation has been decided, train more team members and update protocols and action levels.
- Cascade out training and competence to avoid reliance on expert staff.
- Focus on the pilot project, including impact assessment and the review process, before widespread rollout.
- Communicate rollout to the wider team.

Learning from feedback

- Review implementation after a pre-agreed number of patients and time period (for example, the first 20 patients or three months) and reassess.
- Update, rework and amend training packages and protocols based on the feedback and findings.
- Share experiences with other team members and beyond if appropriate (for example, submit an abstract to an appropriate meeting).

References

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Table A2. Example of 4D CBCT risk assessment

Consequence	Likelihood				
	1 Rare	2 Unlikely	3 Possible	4 Likely	5 Almost certain
5 Catastrophic	5	10	15	20	25
4 Major	4	8	12	16	20
3 Moderate	3	6	9	12	15
2 Minor	2	4	6	8	10
1 Negligible	1	2	3	4	5

1–3	Low risk
4–6	Moderate risk
8–12	High risk
15–25	Extreme risk

Description of risk	Existing control measures	Current risk level Predicted frequency (likelihood) × predicted outcome (consequence) = initial risk score	Control measures to be implemented	Best acceptable risk level Predicted frequency (likelihood) × predicted outcome (consequence) = initial risk score
Increased CBCT dose to patient	Measured/evaluated manufacturer's CBCT parameters	**5 × 3 = 15**	Optimise CBCT parameters	**4 × 2 = 8**
	Define numbers of CBCT acquired in protocol		Limit number of 4D CBCT scans over a course of treatment (eg, 1 × weekly)	
Increased appointment times due to 4D CBCT	Optimise appointment times based on regular audit	**5 × 3 = 15**	Undertake audit of 4D CBCT appointment times during pilot project to assess	**4 × 2 = 8**
	Increase appointment time from 15 mins to 30 mins for 4D CBCT appointments		Review of CBCT to be largely done offline	
			4D CBCT not to be done daily	
			Appointment time will reduce once team familiar with new technique	

Lack of staff experience and understanding of the system and its limitations	Provide training sessions for all core team members who will be involved in implementing 4D CBCT	**4 × 3 = 12**	Monitor number of non-conformances/DATIX related to 4D CBCT to assess trends	**2 × 2 = 4**
	Arrange visit by team implementing technique to another centre using 4D CBCT		Implement in-house training package based on departmental experience	
	Implementation team to write clinical protocol and compare with protocols from other centres, then analyse protocol at regular intervals (at least annually)		Create 'quick guide' to be placed at treatment console	
			Analyse protocol at regular intervals (at least annually)	
	Arrange for core team to have applications training and be available for all 4D CBCT scans during implementation phase			
Increased demands on MPE time	Provide training to ensure that team members only request MPE input where necessary	**4 × 3 = 12**	Monitor during pilot project	**3 × 2 = 6**
			Hold regular meetings with 4D CBCT MDT to assess	
Increased demands on clinician time	Provide training to ensure that team members only request clinical input where necessary	**4 × 3 =12**	Monitor during pilot project	**3 × 2 = 6**
			Hold regular meetings with 4D CBCT MDT to assess	
Availability of 4D CBCT	Not available on all linacs therefore may be unavailable during planned and unplanned downtime	**3 × 2 = 6**	Not acquired daily – encompassed in SOP that standard CBCT can be used where 4D CBCT is unavailable.	**2 × 2 = 4**
Changes to standard operating procedures (SOP)	Approve new protocol and provide staff training on technique; 4D CBCT core team to meet at least monthly before and after implementation	**3 × 2 = 6**	Arrange annual protocol review by 4D CBCT working group	**2 × 2 = 4**

Appendix 14.3. Example of a change form used to manage a radiotherapy project

The boxes would expand or could be added to as required.

Radiotherapy project			
Title		**Ref**	
Ref previous related projects			
Start date		**Estimated end date**	
Stage 1: define goals			
Project description		**Clinical rationale/need (why is it necessary?)**	
Key goals (what would success look like?)		**Team members (indicate leader with *)**	
		Clinical oncologist	
		Radiographer	
		Physics	
		MPE	
		Other	
Stage 2: establish the baseline			
Describe current state		**Identify influencing factors**	
Stage 3: design and prepare			
Risk assessment completed (including radiation considerations)?			
Training requirements		**Funding/resource requirements**	

Actions from risk assessment	Who	Due	Status
Actions to achieve project goals	**Who**	**Due**	**Status**

Stage 4: test and refine			
End-to-end testing		**Review prior to commencing pilot**	
All documentation in place?		**Ready to proceed with pilot?**	
Actions from pilot	**Who**	**Due**	**Status**

Stage 5: full implementation and review	
Feedback and review of successes	**Lessons learned**
Resource implications	**Details of full implementation**
Project closure	

Appendix 14.4. Example of an IGRT training and competency programme

Training must be developed and adapted to meet the needs of departmental processes and site-specific issues. The objective of any training programme must be clearly defined from the beginning.

IGRT training

Composed of a series of multidisciplinary didactic lectures, clinical examples, supporting literature (departmental protocols and relevant journal articles), written information (specific workbook) and hands-on practical experience covering the following.

- **Rationale for IGRT choice:** anatomical site, disease management, anatomy recognition, motion of target volume and OAR, motion management.
- **Acquisition process:** preparing reference image, image parameters/modes, optimising image quality. Training could be supported by using phantom test cases.
- **Image analysis process:** image analysis training and decision-making. Development of image analysis guidelines/protocol/flowcharts to support and direct image review. A database of patient images for different IGRT techniques and anatomical sites should be available for offline practical experience.
- **Action:** guidance on action levels, appropriate interventions, timing of interventions, escalation and justification of exposure.

The use of self-assessment alongside summative assessment is useful to engage and promote self-reflection and measure achievement.

Baseline assessment

- Self-assessment questions evaluating an individual's confidence in specific areas: image acquisition, anatomy recognition, image analysis and decision-making, for example.
- CT/CBCT anatomy recognition pre-test. Delineation of target anatomy, compared against gold-standard reference contour.

Summative assessment

- Database of images, match and decision-making competency assessed against a gold standard. Predefined minimum level of concordance set for clinical competency.
- CT/CBCT anatomy recognition post-test. Delineation of target anatomy, compared against gold-standard reference contour.
- Self-assessment questions (repeated) evaluating radiographer confidence in image acquisition, anatomy recognition, image analysis and decision-making for specific sites.

Maintaining competency

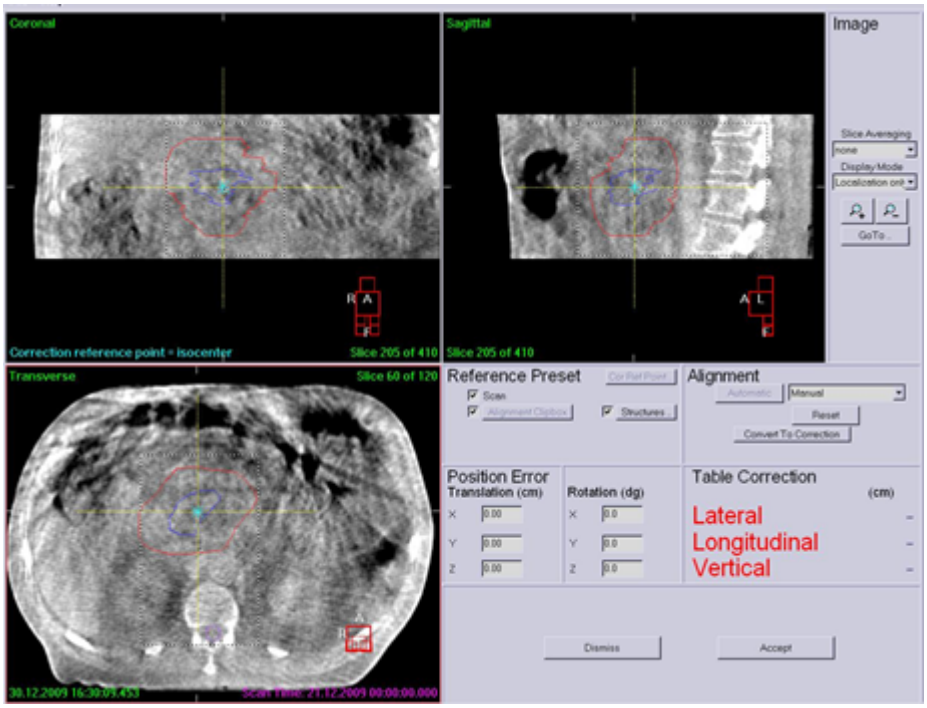
- Upkeep of a portfolio of relevant experience, including self-reflection. Predefined minimum number of case reviews required annually. The number will be a balance between the number of patients treated with that technique and the number of radiographers required to maintain competency. Peer review of portfolio at least yearly.

- If an individual does not meet the minimum number of case reviews due to absence from practice or a period away from radiotherapy treatment or a specific technology, repeat summative assessment, with a second database of images.
- Training updates delivered as required, dependent on treatment practice and imaging practice site changes.

Appendix 14.5. Imaging examples of site-specific issues

Section 10.7.2 Pancreas

Example of excess gas affecting CBCT image quality



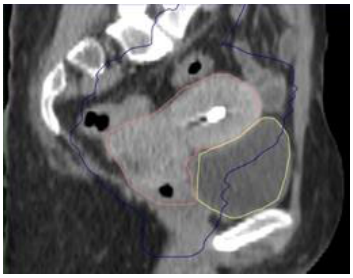
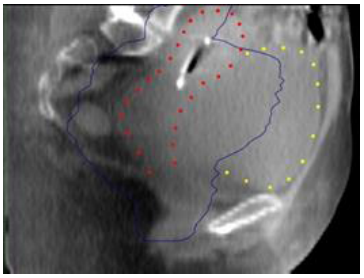
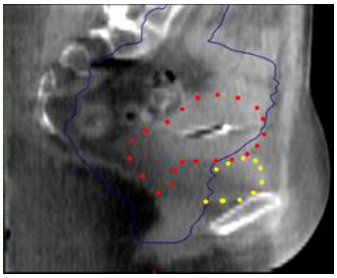
Section 10.9 Gynaecological

1. Bladder volume: example of bladder volume variations affecting target coverage

Image A: planning CT. The PTV is outlined in blue, CTV in red and bladder in yellow.

Image B: fraction 6 CBCT. The PTV is outlined in blue, CTV in red and bladder in yellow. Note the bladder is larger than planned pushing the uterus superiorly.

Image C: fraction 12 CBCT. The PTV is outlined in blue, CTV in red and bladder in yellow. Note the bladder is smaller than planned resulting in the uterus dropping inferiorly.

Image A	Image B	Image C
		

2. Rectal volume: example of rectal volume variations affecting target coverage

Image A: planning CT. The PTV is outlined in blue, CTV in red and rectum in yellow.

Image B: fraction 16 CBCT. The PTV is outlined in blue, CTV in red. Note the posterior shift due to reduction in rectal diameter.

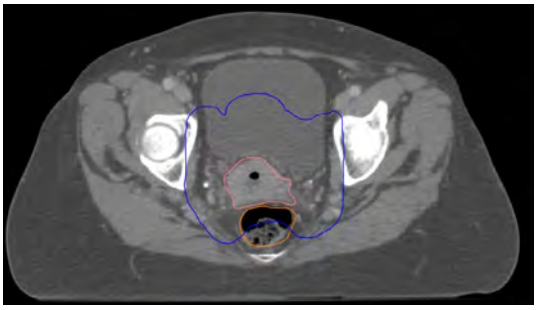
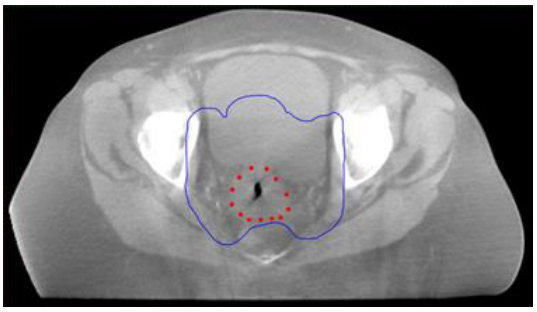
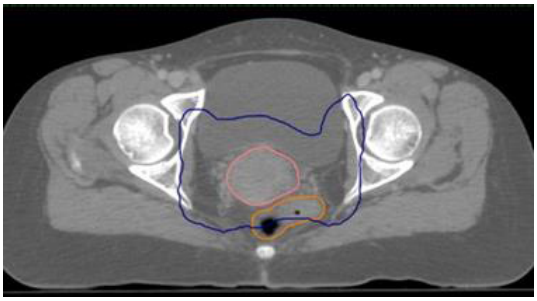
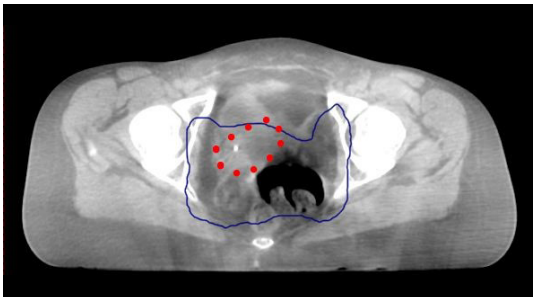
Image A	Image B
	

Image C: planning CT. The PTV is outlined in blue, CTV in red and rectum in yellow.

Image D: fraction 4 CBCT. The PTV is outlined in blue, CTV in red. Note the anterior shift due to increase in rectal diameter.

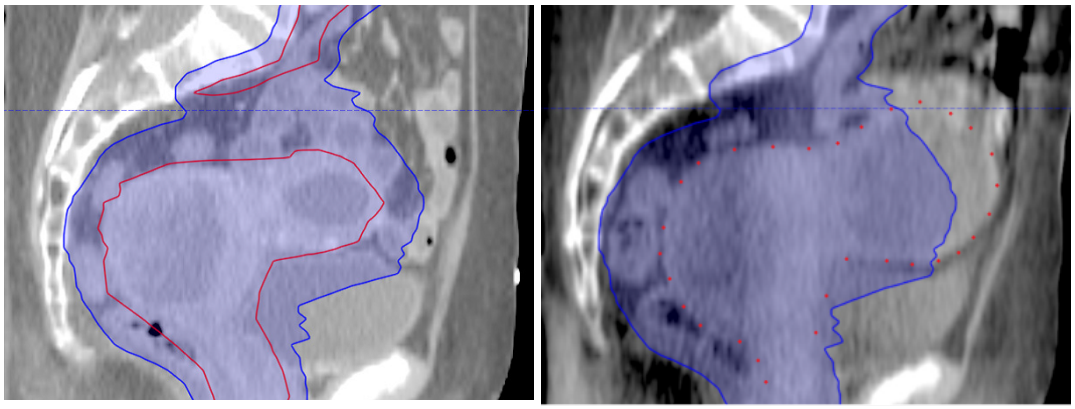
Image C	Image D
	

3. Uterine distention: example of uterine distention affecting target coverage

Image A: planning CT. The PTV is outlined in blue, the CTV in red.

Image B: fraction 1 CBCT. The PTV is outlined in blue, the CTV in red. Note uterus distention causing poor CTV coverage.

Image A	Image B

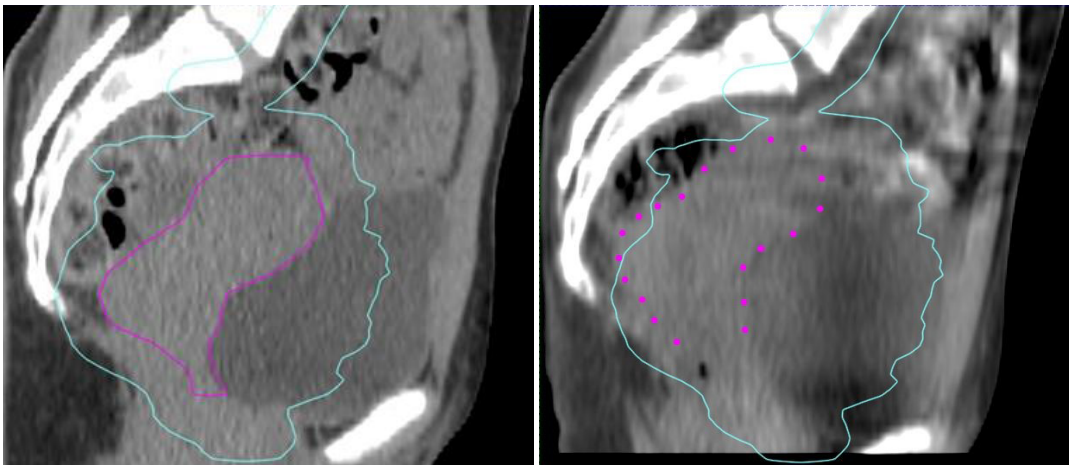


4. Pelvic pitch: effect of pitch on target coverage

Image A: planning CT. The PTV is outlined in blue, the CTV in pink.

Image B: fraction 11 CBCT. The PTV is outlined in blue, the CTV in pink. Note the position of L5 and pubic symphysis; this patient's pelvic tilt was measured to be 8 degrees.

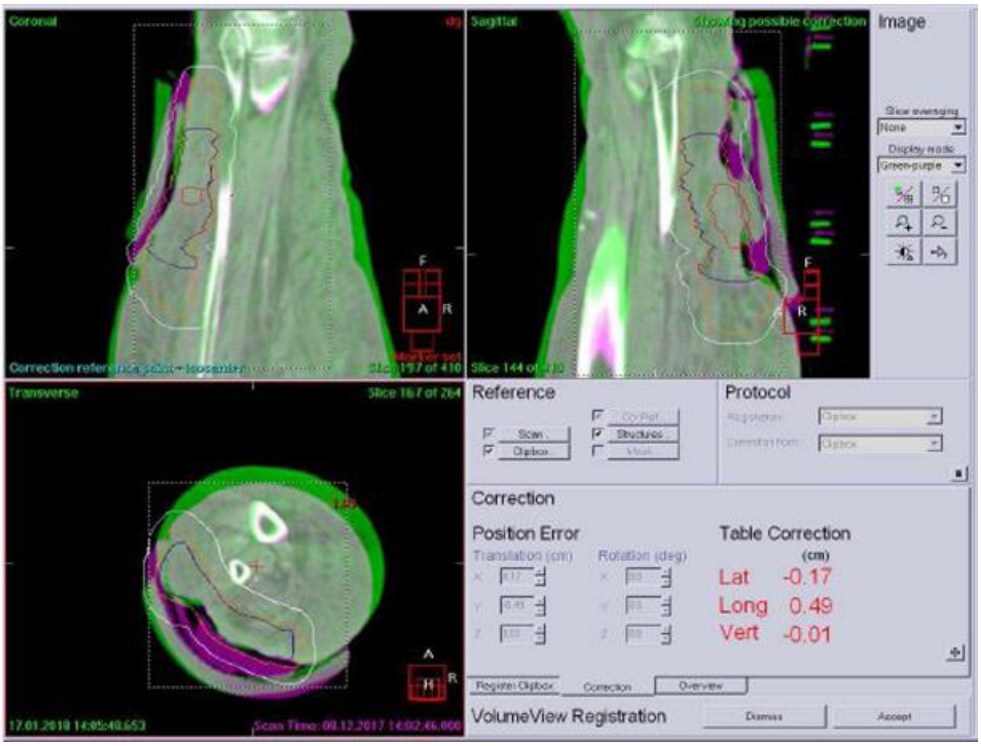
Image A	Image B



Section 10.12 Sarcoma

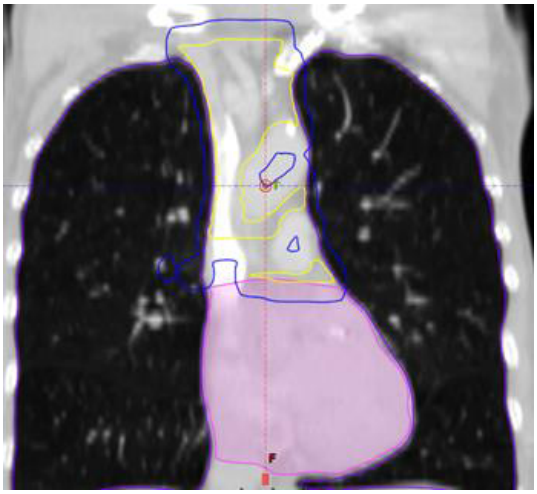
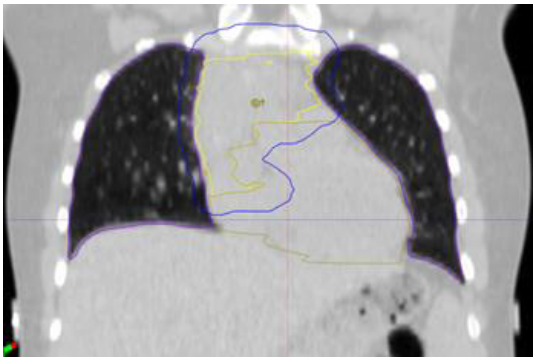
CBCT showing contour change between simulation scan and on-treatment image for a sarcoma in upper leg

Changes at the wound site created problems with bolus placement and there is swelling opposite the PTV. This patient's treatment needed to be replanned. The patient moved from standard weekly imaging to daily imaging due to variable set-up.

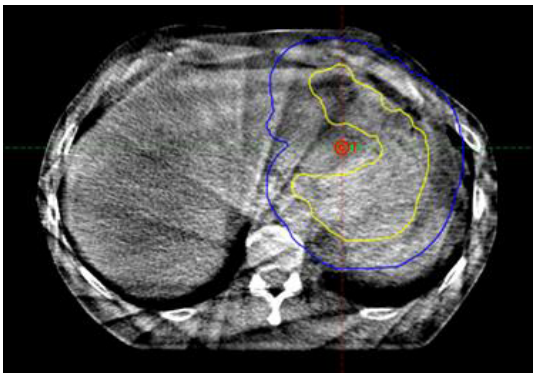
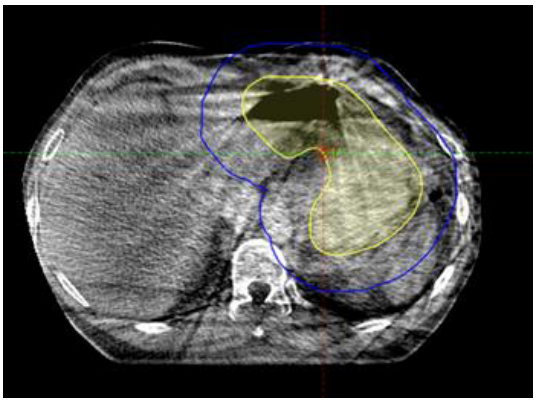
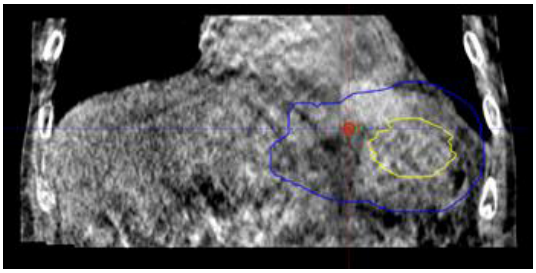
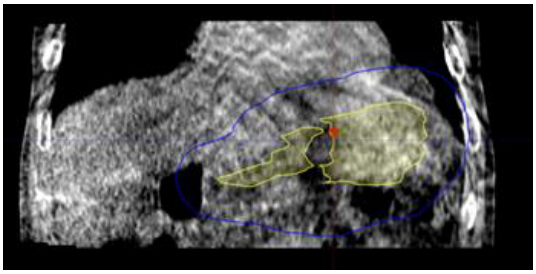


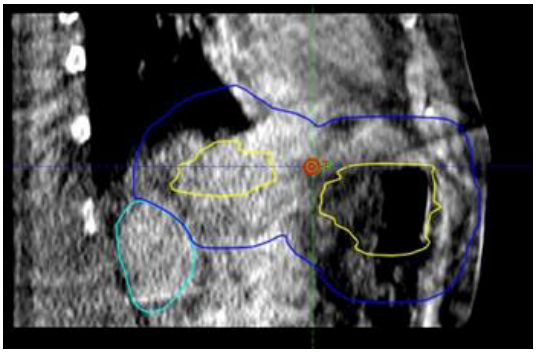
Section 10.13 Lymphoma

1. Example of CBCT for mediastinal radiotherapy

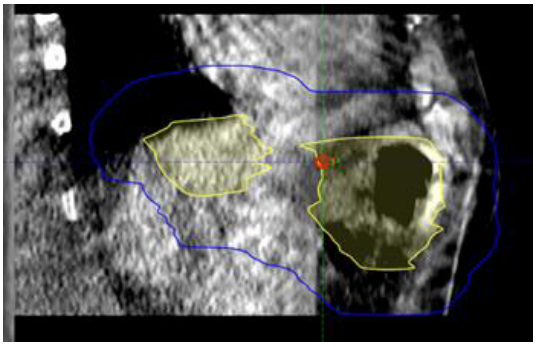
CT in DIBH for mediastinum	CT in FB for mediastinum
	
This CT image was acquired in DIBH. The heart is elongated and pulled inferiorly. In addition, the lungs are inflated more thus reducing the volume of lung irradiated.	This CT image was acquired in FB. It is of a different patient but it can be used to visualise heart and lungs in FB. The heart is more superior compared with CT in DIBH. In addition, the lungs are less inflated.

2. Example of CBCT and stomach radiotherapy

Example of stomach replan	
	
	



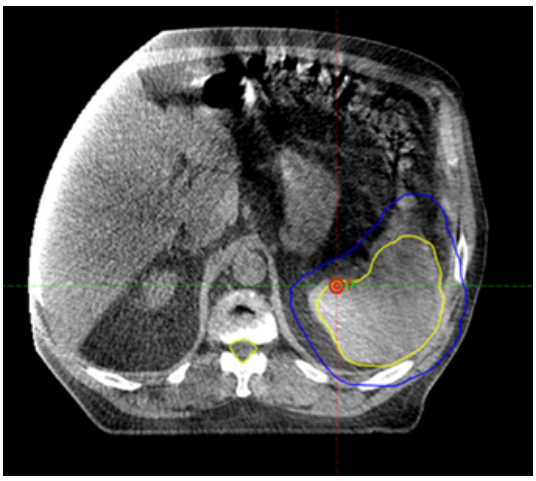
This was the original plan but after five fractions changes occurred and the stomach shape changed. If 2D imaging had been used then this would not have become apparent and could have resulted in a geographical miss despite large planning margins.

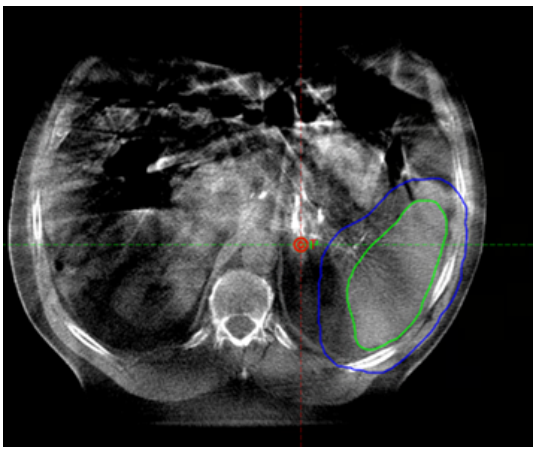


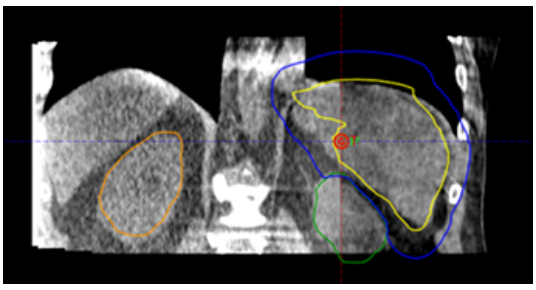
This is the same patient but after a replan. It can be seen that the PTV margins are substantially larger than the original plan.

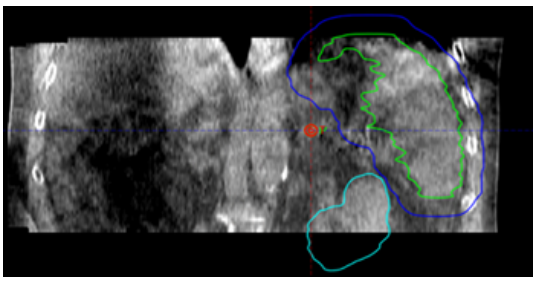
3. Example of CBCT for splenic radiotherapy

CBCT in DIBH for spleen radiotherapy	CBCT in FB for spleen radiotherapy
Blue = PTV, Yellow=CTV	Blue = PTV Green = CTV





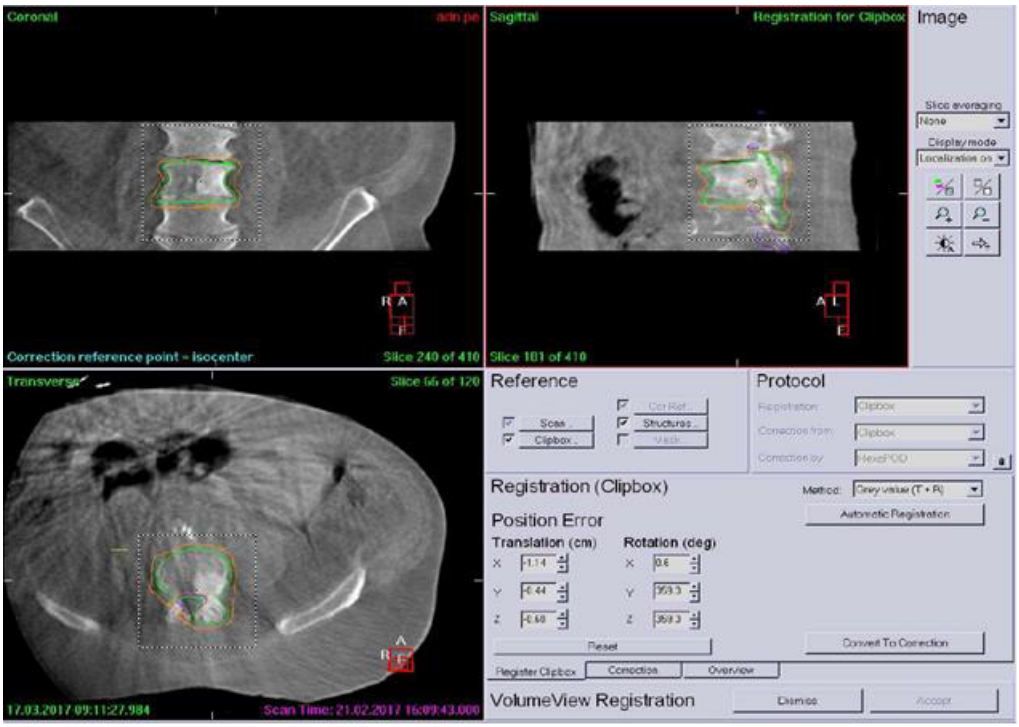




The images above were acquired in DIBH. The image quality is good. The spleen can be seen clearly.	The images above were acquired in FB. Although the image quality is not bad there are more artefacts compared with CBCT in DIBH. In addition there is a greater risk of CTV moving outside PTV during FB compared with DIBH treatment.

Section 10.14 Spinal metastases treatment with SABR

Imaging examples: in larger patients, image quality degradation can occur; a higher CBCT dose should be considered to overcome such degradation. In this case, poor contrast is exacerbated by artefacts from bowel gas.



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The Royal College of Radiologists. *On target 2: updated guidance for image-guided radiotherapy*. London: The Royal College of Radiologists, 2021.

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