National Cancer Action Team
Part of the National Cancer Programme

# National Radiotherapy Implementation Group Report

## Image Guided Radiotherapy (IGRT)

## Guidance for implementation and use.

**August 2012**

Foreword

Image Guided Radiotherapy (IGRT) is a concept that should now be an essential part of all radiotherapy delivered for the treatment of cancer and critical to achieving the aims of delivering a world class radiotherapy service as set out in the Cancer Reform Strategy (2007) and underlined in Improving Outcomes: A Strategy for Cancer (2011).

The principles of the accurate placement of radiotherapy dose to match the intended target volume within the patient align with the fundamental strands of the NHS Outcomes Framework 2011/12. Radiotherapy treatment 'geographical misses' may reduce cure rates (Domain 1 – Preventing people from dying prematurely) and increase the chance of avoidable harm (Domain 5) through increased side effects with direct links to patients' quality of life (Domains 2 and 3).

This document is not designed to be guidance for commissioners. It is primarily a guide for radiotherapy services and professionals to choose and implement appropriate IGRT techniques in different clinical situations to ensure high quality standards. The rapid pace of change in advanced radiotherapy technologies means existing guidance needs revising and updating. This guidance reaffirms the principles and updates On Target: Ensuring Geometric Accuracy in Radiotherapy - 2008

The report, written by some of the leading experts in IGRT across the country makes a number of clear recommendations. It specifies adopting the IGRT protocols set out in this report into clinical practice; having a multi-professional team approach and establishing a lead individual within each service to coordinate IGRT use.

The National Cancer Action Team are currently preparing a programme of support to services to allow the rapid implementation of this report through a team of clinical experts. I would encourage all services in England to take advantage of this resource, and to adopt and implement the protocols set out in this report.

**Professor Sir Mike Richards**
**National Cancer Director**
**August 2012**

**Executive Summary**

The NRAG report, published in 2007, sets out the important role of 4D adaptive radiotherapy (4D-ART), and advanced radiotherapy should become the standard of care. This guidance is written to support the wider adoption and application of Image guided radiotherapy (IGRT) to enable the future implementation of 4D adaptive radiotherapy throughout England.

This NCAT guidance updates the On Target: Ensuring Geometric Accuracy in Radiotherapy report (joint SCOR, IPEM, RCR publication 2008) and particularly introduces emphasis on volumetric and fiducial marker imaging of target volumes where clinically appropriate.

This guidance is designed for radiotherapy professionals of all disciplines in the implementation, choice and use of appropriate IGRT techniques to ensure high quality standards across England. It may also inform commissioners in how advanced radiotherapy can lead to improved outcomes from radiotherapy and how to assess markers of quality standards.

IGRT must not be seen as a standalone intervention. When establishing an IGRT service development strategy the entire process of IGRT (as described in this document) should be considered from radiotherapy planning and throughout treatment.

Every patient should have a form of IGRT as part of his or her radiotherapy treatment episode. The frequency and complexity reflects the treatment intent, anatomical site and fractionation (as detailed in the site specific protocols).

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 include the site treated, the immobilisation used and the patient's condition. These protocols should be based on the generic protocols in this document and make reference to the dose received along with the correction strategies used.

The Specialised Commissioning Group service specification for radiotherapy clearly includes out the importance of IGRT, and this document supports the delivery of this.

'There is access to modern radiotherapy techniques, e.g. Intensity Modulated Radiotherapy (IMRT) and Image Guided Radiotherapy (IGRT). Services not able to offer this will be expected to have plans in place to move to routine IGRT over the next 12 months'

All modern linear accelerators have some IGRT capability.

Few services in England are maximising the potential for IGRT in the routine clinical setting.

IGRT is not a separate clinically delivered service, but rather is an intervention within the treatment pathway to ensure the service is accurately directed and of high quality.

IGRT is a core component of modern radiotherapy services and requires a multi-professional team approach and provides opportunities for expanded professional development. It is the responsibility of each therapeutic radiographer, medical physicist, dosimetrist and clinical oncologist (and all clinical practitioners) to ensure that they maintain their skills as technology evolves.

Although image review is a core skill of all clinical staff it should be performed by the individuals involved in the treatment delivery of the patient imaged.

A good quality image is one that is suitable for the clinical task required and achieved with radiation exposure as low as reasonably achievable.

Every centre should have an IGRT multi-disciplinary team that includes at least one IGRT specialist therapeutic radiographer.

Routine prospective IGRT data collection for the individual patient and individual anatomical sites in a radiotherapy department is essential to calculate the systematic and random errors and inform local margins.

Data collection is one of the most critical aspects to ensure the safe implementation and use of IGRT.

The aim is to ensure that the planned dose is delivered to the tumour. The implications are:

The potential of 'geographical miss': It is clear that without regular imaging and correction, relying on a set of external co-ordinates on the patient's skin, which may only partially correlate to the internal tumour position, the risk of missing the target for some or all of the treatment is high.

The consequences of 'geographical miss': This falls into two main categories; (1) missing the target during the RT course will under dose the tumour and potentially compromise tumour control. (2) potentially increasing the dose to surrounding normal tissues which in turn potentially increases acute and late side effects.

Only once the accuracy of dose delivered to a target volume is established, can IGRT, ideally through research studies or prospective audit, be used to reduce margins or facilitate dose escalation to further improve outcomes.

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

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

The National Radiotherapy Implementation Group (NRIG) has developed a strategy with the National Cancer Action Team for improvement and sustainability of the use of IGRT. Radiotherapy provider organisations are encouraged to engage with this strategy to match the national radiotherapy service specification.

**Glossary**

The Glossary has been inserted early in the document to aid the lay readers interpretation.

| | |
|---|---|
| **4D-ART** | **4D adaptive radiotherapy**<br>4D adaptive radiotherapy is the ability to take account of the tumour shape in the three physical dimensions plus the fourth dimension of change with time. As such, the ability to image the tumour and to visually relate the tumours position (or a surrogate for it) to the radiation field is vital. |
| **4D Imaging** | The fourth dimension is time. 4D imaging is therefore any imaging acquired over a period of time to improve tumour definition, quantify motion and/or changes. |
| **CBCT** | **Cone Beam CT** |
| **CT** | **Computed Tomography** |
| **CTV** | **Clinical Target Volume**<br>The clinical target volume (CTV) is a tissue volume that contains a demonstrable Gross Tumour Volume and/or is considered to contain microscopic, subclinical extensions at a certain probability level. |
| **EPI** | **Electronic Portal Imaging**<br>Electronic portal imaging is the process of using digital imaging, such as a CCD video camera, liquid ion chamber and amorphous silicon flat panel detectors to create a digital image with improved quality and contrast over traditional portal imaging. |
| **Error** | **Set up Error**<br>A mathematical quantity referring to the measured difference between planned (expected) and observed at treatment (actual). |
| **Gy** | **The Gray**<br>**The Gray is the unit of radiation dose measurement** |
| **GTV** | **Gross Tumour Volume**<br>GTV is the macroscopic extent of the clinical growth of the tumour. This includes clinically palpable tumour or tumour identified on imaging. |
| **IGRT** | **Image Guided Radiotherapy**<br>Image Guided Radiotherapy (IGRT) is any imaging at pre-treatment and delivery, the result of which is acted upon, that improves or verifies the accuracy of radiotherapy. IGRT encompasses the whole range from simple visual field alignment checks, through to the more complex volumetric imaging that allows direct visualisation of the target volume and surrounding anatomy. |

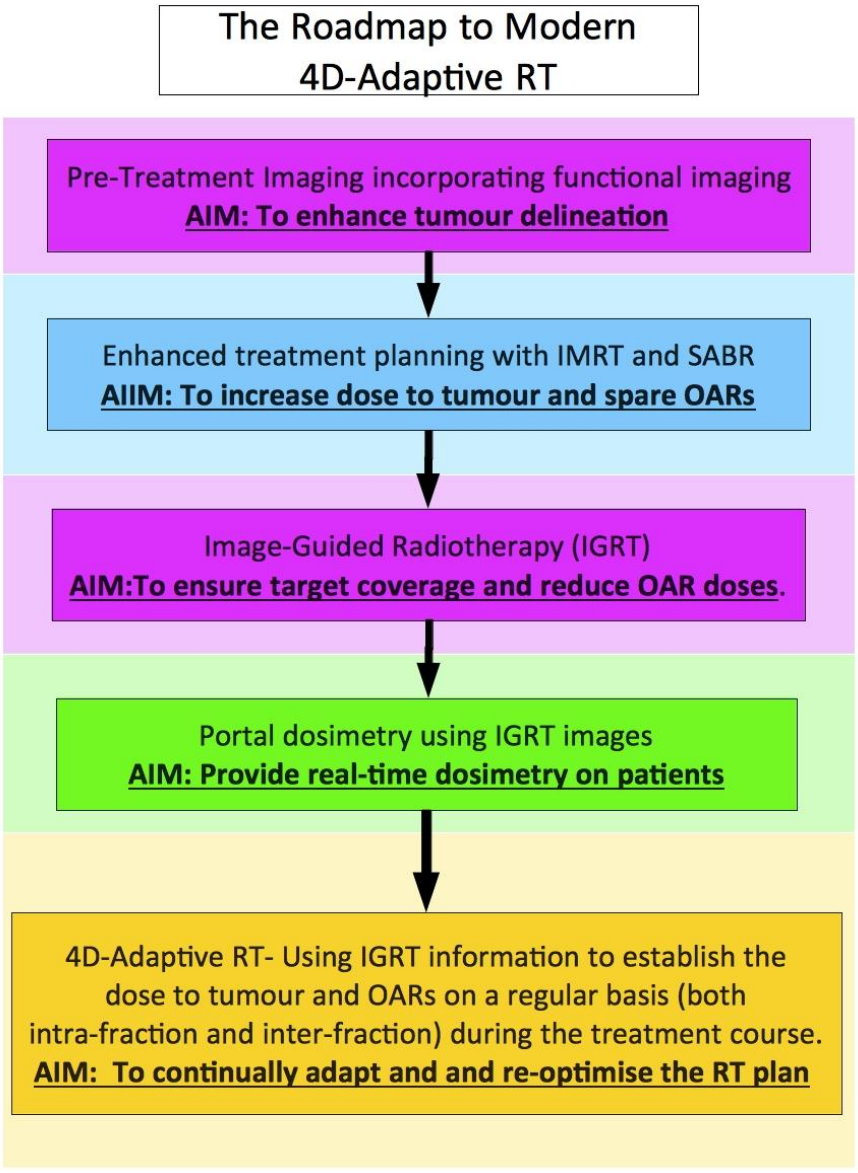
| | |
|---|---|
| **IMRT** | **Intensity Modulated Radiotherapy**<br>IMRT is a high precision form of radiotherapy. It conforms the shape and dose of the radiation precisely to the volume of tumour tissue that needs to be treated. |
| **ITV** | **Internal Target Volume**<br>The internal target volume (ITV) is the volume encompassing the CTV, which takes into account the fact that the CTV varies in position, shape and size |
| **kV** | **Kilovoltage** |
| **MV** | **Megavoltage** |
| **OAR** | **Organs at Risk**<br>Organs at risk are normal tissues (e.g. spinal cord) whose radiation sensitivity may significantly influence treatment planning or prescribed dose. |
| **PET** | **Positron emission tomography**<br>An imaging technique that uses short-lived radioactive substances to produce three-dimensional images of those substances functioning within the body. |
| **PTV** | **Planning Target Volume**<br>The planning target volume (PTV) is a geometric concept, used for treatment planning, and it is defined to select appropriate beam sizes and beam arrangements, to ensure that the prescribed dose is actually delivered to the CTV. |
| **SBRT/SABR** | **Stereotactic Body Radiotherapy/Stereotactic Ablative Radiotherapy**<br>Stereotactic body radiotherapy (SBRT) or Stereotactic Ablative Radiotherapy (SABR) refers to the precise irradiation of an image defined extra cranial lesion associated with the use of high radiation dose in a small number of fractions". |

## 1.0. Introduction

1.1. The NRAG report[1] was published in 2007 and accepted by Ministers. This set the national strategy for radiotherapy and has been the template for development of services. The expectation in the NRAG report was that 4D adaptive radiotherapy (4D-ART) would become the standard of care: **[*NRAG advises that image guided four-dimensional (4D) adaptive radiotherapy is the future standard of care for radical radiotherapy treatment that the NHS should aspire* to]**. NRAG also set out that 3D planning is the standard of care

1.2. This guidance is written to support the wider adoption and application of Image guided radiotherapy (IGRT) to enable the future implementation of 4D-ART throughout England.

1.3. As shown below the roadmap to 4D-ART involves many key stages and is currently not available in routine radiotherapy practice. This document focuses on the IGRT component, (highlighted in purple) an essential requirement to perform 4D-ART.



1.4 This guidance is complementary to the On Target: Ensuring Geometric Accuracy in Radiotherapy[2] report (published by the three professional bodies). 'On target' has defined the principles of geometric verification and the determination of margins; this document builds on these principles to include the new technology which has become available.

1.5 This guidance is aimed primarily at clinicians of all disciplines (Oncologists, Radiographers, Dosimetrists and Physicists) in the implementation and use of suitable IGRT techniques. This is also written for commissioners to support its appropriate use to improve outcomes from radiotherapy.

**Definition**

*Image Guided Radiotherapy (IGRT) is any imaging at the pre-treatment and treatment delivery stage that leads to an action that can improve or verify the accuracy of radiotherapy.*
*IGRT encompasses a wide range of techniques ranging 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.*

**References**


1 Radiotherapy: Developing a World Class Service for England – Department of Health 11th May 2007.
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_074575

2 On Target: Ensuring Geometric Accuracy In Radiotherapy. A joint report published by the Society and College of Radiographers, the Institute of Physics and Engineering in Medicine and The Royal College of Radiologists.
http://www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=292

## 2.0 Commissioning Intention

2.1 Radiotherapy will be commissioned, as a minimum, through specialised services commissioning beyond April 2012. IGRT is recognised through the Service Specification to be the important standard of radiotherapy delivery assurance. The commissioning strategy links the uptake of IMRT and IGRT with improvements in outcomes.

2.2 IGRT clearly relates to the DH outcomes framework, particularly Domain 5 (treating and caring for people in a safe environment and protecting them from avoidable harm) where IGRT ensures accurate delivery of the treatment as planned; but also in Domain 3 (helping people to recover from episodes of ill health) with its role in minimising normal tissue irradiation. However, IGRT also has the potential to impact on Domains 1 and 2.

2.3 The Service Specification sets out

- There is access to modern radiotherapy techniques, e.g. Intensity Modulated Radiotherapy (IMRT) and Image Guided Radiotherapy (IGRT). Services not able to offer this will be expected to have plans in place to move to routine IGRT over the next 12 months.

## 3.0 IGRT and its importance as the standard of care.

3.1 The national strategy for radiotherapy described in Improving Outcomes: A Strategy for Cancer[3] sets out that: access to radiotherapy is critical to improving outcomes and, to improve outcomes from radiotherapy, there must be equitable access to high quality, safe, timely, protocol-driven quality-controlled services focused around patients' needs.

3.2 It also sets out that improved outcomes can also be delivered by ensuring that patients have access to high quality modern radiotherapy techniques, comparable to those used in other European countries, to improve cure rates and improve patients' experience by minimising any long-term side effects of treatment.

3.3 Ensuring accuracy, reducing normal tissue toxicity and minimising side-effects are all key steps in improving outcomes.

3.4 The NRAG report set out that 4D adaptive radiotherapy is the standard of care for radiotherapy. IGRT is the key component of 4D adaptive radiotherapy. 4D adaptive radiotherapy is the ability to take account of the tumour shape in the three physical dimensions plus the fourth dimension of change with time. As such, the ability to image the tumour and to visually relate the tumours position (or a surrogate for it) to the radiation field is vital.

3.5 IGRT is therefore the standard of care that should be applied to all patients as identified in this report.

**References**

3 Improving Outcomes: A Strategy for Cancer - First Annual Report 2011 – Department of Health 13th December 2011
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_131690

## 4.0 The Radiotherapy Pathway

4.1 In the past decade there have been significant advances in all aspects of the radiotherapy pathway.

**4.2 We can now IDENTIFY the target better prior to treatment:**

- Computed Tomography (CT) planning is now standard for all radical and most palliative cases.
- PET/CT and MRI/CT Fusion - combining imaging modalities to enhance the ability to define the radiotherapy target more clearly.
- 4DCT scanning, where the 4th dimension refers to time. At CT planning a 4D CT scan can allow mobile tumours to be identified more clearly and the amount of motion quantified.
- Functional imaging allows more active tumour areas to be identified and can be used to assess the response to radiotherapy allowing for plan to be adapted to the individual patient's needs.

**4.3 We can now PLAN radiotherapy and DELIVER radiotherapy better:**

- Intensity Modulated Radiotherapy now allows the radiotherapy dose to be "modulated" using many more radiotherapy fields. This allows the radiotherapy dose to be delivered to the tumour whilst reducing the dose to close critical normal tissues. This can increase the chance of tumour control and/or reduce the acute and late side effects of radiotherapy.
- Stereotactic Ablative Radiotherapy (SABR) or Stereotactic Body Radiotherapy (SBRT) allows for very precise irradiation of tumours in a small number of large radiotherapy doses. This increases the biological effect of the radiotherapy, improving the chance of tumour control yet minimising the dose to normal tissues.

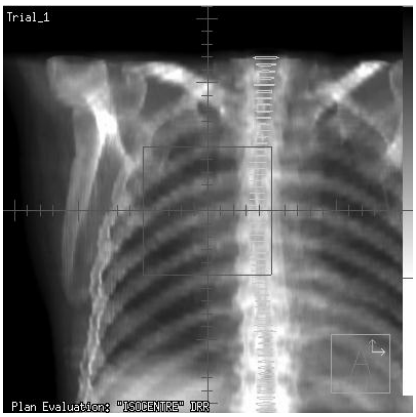
**However, to achieve the optimum cancer outcome for the patient we need to ensure that we HIT the target with the radiotherapy on a daily basis- i.e. Image Guided Radiotherapy (IGRT).**

4.4 **Ensuring ACCURATE radiotherapy**

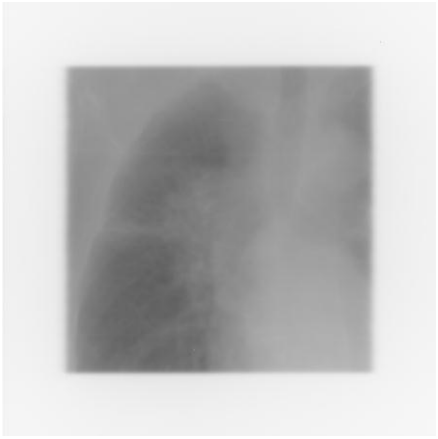
- Traditionally a patient is CT scanned 1-2 weeks before they start radiotherapy and multiple tattoos are performed so the patient's external anatomy can be aligned accurately when they come back for their radiotherapy treatment. If external tattoos are to be solely relied upon for accuracy we must assume that the patient's external anatomy is constant and that the target inside the patient remains in the same position every day in relation to the external anatomy.
- This is not the case: not only can a patient's external anatomy change during treatment (e.g. due to weight loss) but there is also considerable evidence that the internal tumour moves independently of the external anatomy during a radiotherapy course.
- Therefore some IGRT has been used since the 1980's to improve the accuracy of treatment delivery. As with all other aspects of radiotherapy, recent innovations in imaging and computer software now allow much more detailed images of the patient to be acquired on the linear accelerator.
- The complexity of the imaging required depends on the anatomical site to be treated.
- In some tumour sites, e.g. brain, the bony anatomy is a reliable and accurate surrogate for the tumour position.
- However, many tumours move independently to the bony anatomy due to internal organ motion. For these tumours, e.g. lung and prostate cancers, 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 (as a proxy for the tumour).
- It is important to remember that ALL modern linear accelerators have some IGRT capability.
- IGRT can be split into planar (i.e. 2D) imaging, volumetric (i.e. 3D) imaging or imaging over time (i.e. 4D) during the radiotherapy treatment. In addition, for some anatomical sites implanted fiducials (in or near the target) can be used to localise the treatment.

4.5 <u>Planar (2-dimensional) Imaging</u>

- 2D imaging is when 2 or more planar images are acquired, typically but not exclusively, at 90 degrees i.e. anterior/posterior and lateral. This allows measurements in all three directions (superior/inferiorly, laterally and anterior-posteriorly) of the target or more usually the bony anatomy.
- Planar imaging with megavoltage (MV) electronic portal imaging (EPI) is a standard feature on most conventional linear accelerators. However images acquired with high megavoltage energies have certain characteristics due to the higher energies used. In particular, the contrast between bone, soft tissue and air seen with conventional x-ray imaging (i.e. kV) is not seen at higher megavoltage energies. See figure 1



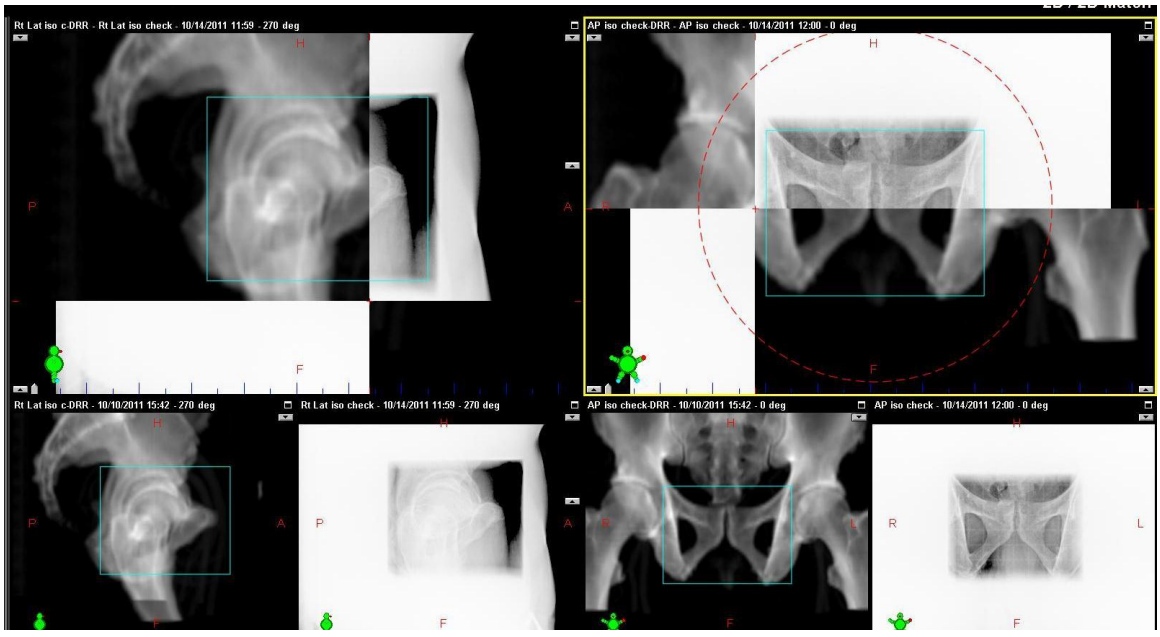

(a)



(b)

Figure 1 AP DRR kV (a) and MV (b) image of thorax

- Planar 2D imaging with kilovoltage (kV) EPI is available on linear accelerators with kV cone beam (Figure 2) and may also be acquired using a system independent of the linac gantry, for example, a tube and detector system mounted on the floor and ceiling.




(b)

Figure 2 Lat and AP DRR and kV image of pelvis

4.6 Volumetric (3-dimensional) Imaging

Volumetric imaging allows for a 3D image to be acquired on the patient in the treatment position on the linear accelerator prior to or during radiotherapy. This enables the internal structures to be visualised including the target and surrounding normal tissues. There are four methods of obtaining a volumetric image on the linear accelerator:

- Cone Beam CT (CBCT): For most standard linear accelerators (see figure 2) volumetric imaging is available via cone beam CT technology which is a kV tube mounted at 90 degrees to the linac head (as shown in figures 3 and 4) and is rotated around the patient using the linac gantry. Both the treatment head (MV) and the CBCT system (kV) have portal imaging capability. It is worth noting that some Linacs have MV conebeam.

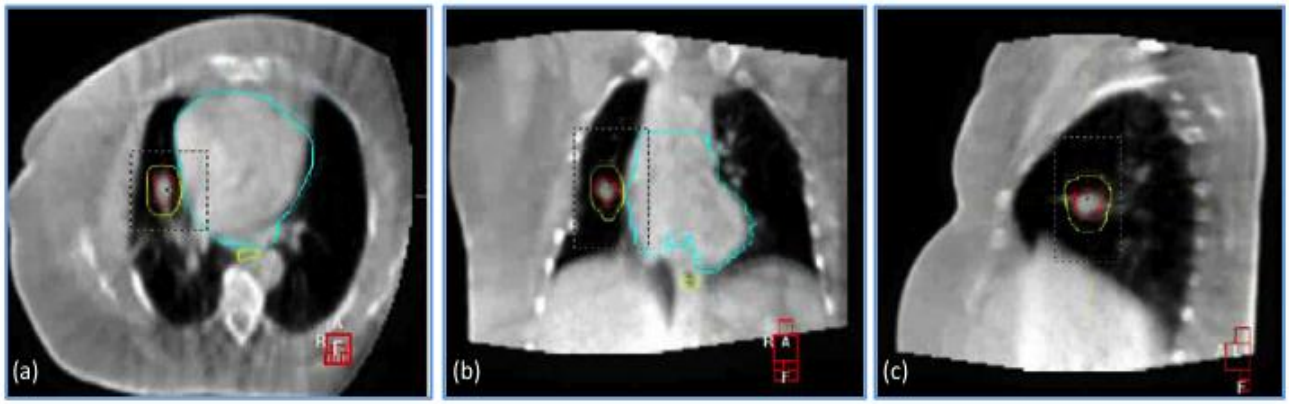



Figure 3 shows a kV CBCT of a SBRT patient in the axial (a), coronal (b) and sagittal (c) planes. These images demonstrate CBCT's ability to match to the tumour and visualise close OARS (e.g. pericardium)

- Megavoltage CT: Uses a megavoltage energy fan beam to create a volumetric image for verification with helical scanning as used in conventional CT imaging (Figure 4).

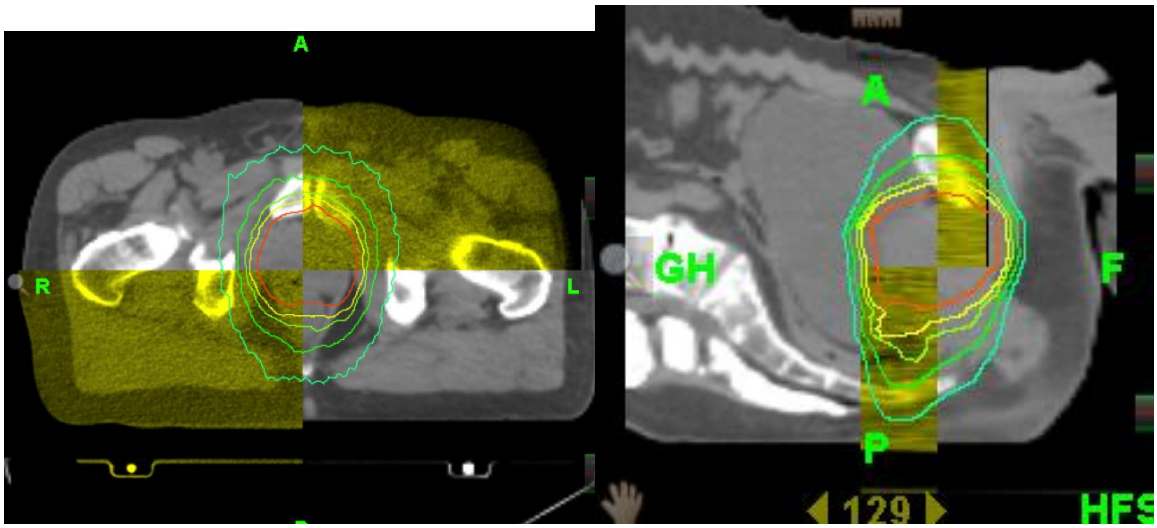
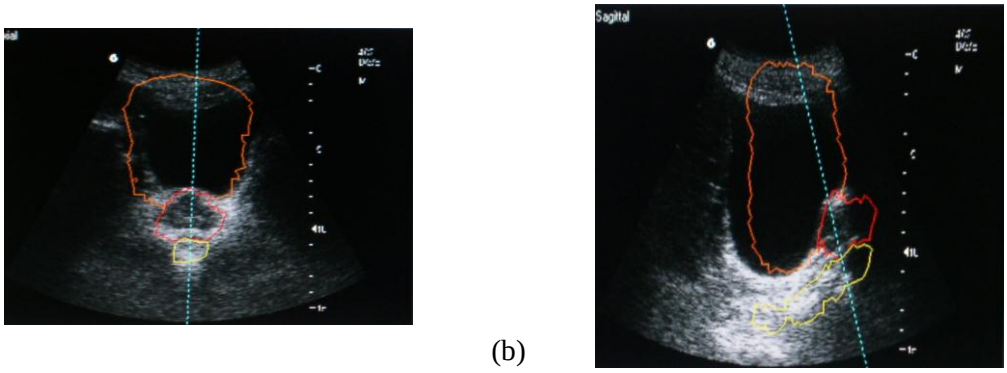



Figure 4. Images demonstrate checkerboard matching and isodose overlay with TomoTherapy™. The grey is the kV planning scan and the yellow is the daily MVCT.

- CT on rails: Consists of a CT scanner in the same room as the linac. The patient couch can be rotated at 180 degrees to transfer from linac to CT

- Ultrasound: Ultrasound probes can provide volumetric images for IGRT in prostate and breast cancer (figure 5)




(a) (b)

Figure 5 Axial (a) and Sagittal (b) ultrasound of prostate with overlay of CT outlines

4.7 Four Dimensional (4D) Imaging

- 4D imaging, i.e. imaging the tumour or surrogate over time can be used before radiotherapy treatment to quantify tumour motion and during the treatment to track tumour motion.

- Kilovoltage (kV) fluoroscopy and 4D CBCT can allow the tumour motion to be quantified before radiotherapy treatment and checked. In addition, kV and MV fluoroscopy can be used during radiotherapy to track the tumour or more commonly, track implanted fiducials placed in or near to the tumour.

4.8 Fiducial markers

- To fully exploit many of these technologies it is necessary for markers to be implanted in or near the tumour or tumour bed. These can either provide additional information in the images acquired, for example CBCT, or be used as a surrogate for target position in planar imaging where soft tissue information is not available.

4.9 Whilst the technology available and potential applications of modern IGRT are new, it is important to clarify that the appropriate level of IGRT should initially be used to ensure that an institution's current RT technique and margins are acceptable.

4.10 The aim is to ensure that the planned dose is delivered to the tumour. Only once this is established, can IGRT, ideally through research studies or prospective audit, be used to reduce margins or facilitate dose escalation.

**SUMMARY: The potential and consequences of missing the tumour.**

**The potential of miss:**
This is well defined in 'On Target'. It is clear that without regular imaging and correction, relying on a set of external co-ordinates on the patient's skin, which may only partially correlate to the internal tumour position, the risk of missing the target for some or all of the treatment is high.

**The consequences of miss:**

This falls into two main categories; (1) missing the target during the RT course will under dose the tumour and potentially compromise tumour control. (2) potentially increasing the dose to surrounding normal tissues which in turn potentially increases acute and late side effects.

## 5.0 Current Position

5.1 Despite the publication of On Target in 2008 the current uptake of IGRT is still variable. This was highlighted by a survey undertaken during the summer of 2011.

5.2 A total of 55 centres responded. The results are reproduced in appendix IV.

5.3 The key points are:

- Over 40% of centres reported having no IGRT facilities other than MV portal imaging.
- For many centres, imaging occurs (in whatever format used) on day 1 only, and then only if patient set up changes.
- In around 40% of centres, clinical protocols did not specify dose values for the exposure when imaging.
- The major factor preventing services from calculating individualised site and centre setup margins was stated as lack of trained staff.

5.4 The aim of the document is to provide local services with recommendations on how IGRT should be implemented and used **now**. However, like all aspects of radiotherapy IGRT is a constantly evolving field with new technological developments becoming available.

## 6.0 The Future

6.1 Developing an appropriate IGRT capability requires a vision of the future. Increasingly, MR and PET are used to aid tumour delineation at planning and in the future MRI and PET equipped linear accelerators will be available. Technology will continue to improve and therefore there is the need to develop class solutions to deal with the multiple modalities of current and future IGRT implementation.

6.2 In addition, as proton facilities become available in the UK, we envisage that the current level of linac based IGRT should be considered as the minimum standard for proton centres. This includes the provision of volumetric imaging, the potential to match to implanted fiducials and the possibility of gated delivery. The site-specific guidelines detailed below will be applicable to proton based RT and should form the basis of proton IGRT.

6.3 This document has therefore been written as a framework for the reader to apply, rather than giving a single solution. The processes and applications are detailed, but so too is the concept and the rationale to allow this to be implemented in new and emerging technologies.

6.4 It is clear that technology will drive change. The clinical radiotherapy community and commissioners must therefore work with the manufacturers of radiotherapy equipment to ensure that IGRT implementation is mirrored through this document.

## 7.0 Commissioning of services and the uptake of IGRT

7.1 This document is written as a guide for clinicians and providers, and therefore does not specifically address commissioning issues. However, the following points are important in a commissioning context.

7.2 IGRT is not a clinically delivered service, but rather is an intervention to ensure the clinically delivered service is accurately directed. As such, commissioning for IGRT should be seen as a quality intervention on a cancer pathway rather than as a standalone clinical service

7.3 The Service Specification proposed to the National Specialised Commissioning Group for radiotherapy sets out a number of standards for IGRT. Whilst it must be recognised that these were written before this guidance document was published, they are seen as valid.

7.4 Clearly commissioners (in the future this is expected to be the National Commissioning Board) will wish to work with providers of services to ensure that IGRT capability is available and that these services offer the opportunity for patients to benefit from this technology.

7.5 Local data collection and reporting will be increasingly important as discussions on IGRT delivery become a regular part of service review. Providers are encouraged therefore to develop local systems for collecting these data to support robust information exchange with commissioners.

7.6 All patients require a certain level of IGRT. For some tumour sites volumetric imaging is essential and should be the standard of care. Providers should understand and assess the impact of this using locally developed protocols based on the guidance in this document.

## 8.0 The Reason for IGRT

8.1 Radiotherapy planning and treatment delivery is a chain of events where discrepancies (or geometric errors) between the planned intended treatment (created from the CT scan) and the treatment delivered can occur. These discrepancies can occur when defining the target volume, creating the treatment plan or differences in patient position at treatment. To compensate for these discrepancies a 'safety' margin is added around the tumour volume delineated on the CT scan to compensate. The International Commission on Radiation Units and Measurements has defined the volumes to be used when creating margins in its reports 50, 62 and 83.

These are:-

- Gross Tumour Volume (GTV) - the primary tumour volume.
- Clinical Target Volume (CTV) - to include GTV and possible microscopic disease.
- Planning Target Volume (PTV) - to account for geometric errors between planning and treatment.

- Internal Target Volume (ITV) – is a component of the PTV, and is the volume encompassing the CTV, which takes into account the fact that the CTV varies in position, shape and size.
- Planning organ at Risk Volume (PRV) - the margin around organs at risk (OAR) to compensate for movements and changes in shape and or size, as well as set up uncertainties.

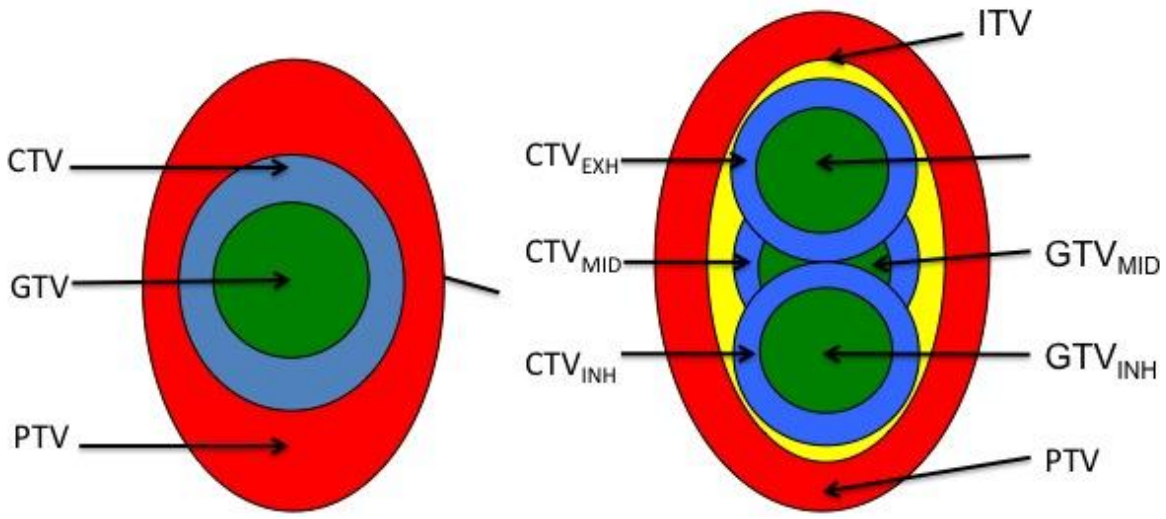



Figure 4. The left image shows a standard scenario where the GTV (green) is expanded to CTV (blue) to account for microscopic spread. An additional margin is added to for set up variation (including any motion) to create the PTV (red). On the right is a patient planned using a 4DCT planning scan. There are various methods to generate the ITV (yellow) but in this example the GTVs (green) at mid ventilation and the extremes of motion are expanded for microscopic disease to create their respective CTVs (blue). The union of these CTVs is used to create the ITV with a smaller margin added to create the PTV (red).

8.2 The use of IGRT strategies have the potential to reduce the errors arising from differences in patient and tumour position from the intended treatment and hence reduce the PTV margin. Typically a patient's radiotherapy plan is based on one planning CT scan. However, this scan is only a 'snapshot' of the patient and position, i.e. it is acquired on one day and at one time. Patient and/or tumour changes can either occur daily (inter-fraction motion) or during the treatment delivery (intra-fraction motion). To account for this larger margins are added to the PTV. However, the addition of margins to the tumour target volume increases the volume of normal tissue treated and can also increase the dose to organs at risk. For example for a prostate of volume ~60cm$^3$ reducing the margin from 10mm to 5mm or 3mm results in a 55% or 74% reduction of normal tissue irradiated, respectively.

8.3 Prior to imaging, the first step in reproducing the patient's position is to align the patient using skin marks/shell marks/external markers, and in-room lasers. The treatment isocentre

is then measured from these reference marks when in alignment. However skin is mobile and early reports showed that the addition of EPI to skin mark positioning decreased the proportion of treatments given with a field-placement error relative to bony anatomy of > or = 5 mm from 69% to 7%[4].

8.4 However, using EPI alone there is an assumption of a constant relationship between bony anatomy position and tumour position. This is not always the case, for example it has quite clearly been demonstrated in patients treated for prostate and lung cancer[5]. The alternatives include using implanted markers to identify the position of the soft tissue or use soft tissue imaging which provides 3D information, for example in-room CT, cone beam or MV CT or in room MRI.

8.5 3D soft tissue or volumetric **i**maging has the additional advantage of identifying anatomical changes during the course of radiotherapy treatment. This is beneficial in lung cancer, for example, where tumour changes during the course of radiation can cause the tumour to move from the original position and without adjustment would lead to a geographical miss[6]. In head and neck cancer[7], changes in the parotid gland in the early stage of the radiation treatment have led to significant dose changes to the OAR's compared to the calculated treatment planning dose. To deliver accurately the radiotherapy treatment, frequent imaging in the treatment position including target and organs at risk is needed. Adjustments can be made to the patient position to compensate for these changes or where more complex changes occur the treatment may need to be replanned.

**References**


4 Gildersleve J, Dearnaley DP, Evans PM, Swindell W. Reproducibility of patient positioning during routine radiotherapy, as assessed by an integrated megavoltage imaging system. Radiother Oncol. 1995 May;35(2):151-60. PubMed PMID: 7569024.

5 Erridge SC, Seppenwoolde Y, Muller SH, van Herk M, De Jaeger K, Belderbos JS, Boersma LJ, Lebesque JV. Portal imaging to assess set-up errors, tumor motion and tumor shrinkage during conformal radiotherapy of non-small cell lung cancer. Radiother Oncol. 2003 Jan;66(1):75-85. PubMed PMID: 12559524.

6 Sonke JJ, Lebesque J, van Herk M. Variability of four-dimensional computed tomography patient models. Int J Radiat Oncol Biol Phys. 2008 Feb 1;70(2):590-8. Epub 2007 Nov 26. PubMed PMID: 18037579.

7 Polat B, Wilbert J, Baier K, Flentje M, Guckenberger M. Nonrigid patient setup errors in the head-and-neck region. Strahlenther Onkol. 2007 Sep;183(9):506-11. PubMed PMID: 17762925.

## 9.0 Reproducibility and Immobilisation

9.0 Achieving reproducibility during radiotherapy planning and treatment can involve reducing motion in both patient bony anatomy and internal organ motion. This may complement or even reduce the need for intensive IGRT techniques. For effective reproducibility the entire process from positioning the patient to setting the isocentre must be considered. The issues that arise are often from basic practice and procedure and are fundamental to the process of improving accuracy but can sometimes be overlooked in the high technology environment of radiotherapy.

9.1 A rigid couch top surface is essential at each stage of the planning and treatment process ensuring conformity between imaging, planning and treatment equipment. External immobilisation systems should ideally attach to the couch top in a unique position in an attempt to avoid daily variation in both patient repositioning and couch sag due to the patient's weight distribution. This indexed patient positioning also enables Oncology Management Systems to give a reliable indication of set up accuracy during the course of treatment.

9.2 Immobilisation aids not only help the patient maintain the required consistent position but may also achieve an advantageous treatment position to reduce dose to normal tissue. However the benefit of these devices can be affected by the skill of the clinical staff making and/or positioning the devices and the co-operation of the patient. Although there are many trials assessing the use of such devices there are few randomised trials. The most vital component of an accurate and reproducible treatment position is that the patient is comfortable and the position can be easily reproduced by both therapeutic radiographer and patient. Sometimes it is better to have a simple system rather than an over complex system. However it is important that each department evaluates the effectiveness of the immobilisation used.

9.3 Methods to reduce internal organ motion can include breathing techniques for breast and thorax cancer patients or bladder and bowel preparation for pelvic patients. Any of these techniques requires adequate patient information and cooperation whilst allowing the patient time to practise. Whatever technique is used the effectiveness should be audited.

9.4 To compensate for the motion, techniques such as 4D scanning, gating and or tracking can be used. The reproducibility of these techniques must be verified to detect any changes in either pattern of breathing or the relationship between any surrogate or external marker used and the tumour. Similarly the effectiveness of these techniques must be reviewed in each department

## 10.0 Image Guided Radiotherapy Protocols

10.1 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 include the site treated, the immobilisation used and the patient's condition.

10.2 The methodology for this is described in detail in the 'On Target' document and is summarised below.

10.3 For radiotherapy treatments set-up errors can be divided into **gross**, **systematic** (Σ) and **random** (σ) errors.

10.4 **Gross errors** should be detected prior to starting the radiotherapy treatment, firstly by viewing the field on the patient (where possible), and secondly, acquiring an image and reviewing prior to delivering the 1$^{st}$ radiotherapy fraction. Therapeutic radiographers should use their professional judgement with this review and can choose to use the matching tools or visually verify the image depending on the image quality, treatment intent and condition of the patient at the time. Ideally when any further images are taken a visual check is made for gross errors.

10.5 **Systematic** errors are reproducible, consistent errors, occurring in the same direction and of similar magnitude. These may occur at the start of radiotherapy or during the course of treatment.

10.6 The **systematic error in set up for an individual patient ($m_{ind}$)** is the mean of a set of displacements. It is calculated by summing the set-up displacements (**without correction)** in the superior/inferior, lateral and anterior/posterior direction for all the images acquired and then dividing this by the number of imaged fractions.

10.7 For example, if three imaging sessions are used, the systematic error in the superior-inferior direction (X) is determined by summing the displacements at the 1st ($X_1$), 2nd($X_2$) and 3rd($X_3$) fraction and dividing this number by 3.

10.8 A **random** error however, varies in direction and magnitude for each delivered treatment fraction. Random errors can also arise from changes in target position, and shape, between fractions and during treatment delivery.

10.9 It is important to remember that **systematic errors** will cause a shift of the dose distribution with respect to the target whereas **random errors** will cause a "blurring" of the dose distribution around the target.

10.10 Multiple images are required to quantify **Systematic** and R**andom** error magnitude. Correction for these errors can be made using a variety of strategies.

10.11 The **systematic error** ($m_{ind}$) for an individual can be generalised for n number of imaged fractions :

$$m_{ind} = \frac{(X_1 + X_2 + X_3 + X_4 + .....X_n)}{n}$$

10.12 The patient random error (σind) is any variation in set-up on each individual fraction. It is the standard deviation of the measured errors and describes the variation of the individual measurements about the mean.

For set up variations $X_1$, $X_2$, $X_3$……$X_n$ where 1, 2, 3 to n are imaged factions and the mean of the data is $X_{mean}$, the standard deviation (random) error is given by :

$$\sigma_{ind} = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(X_i - X_{mean})^2}$$

10.13 These equations refer to individual patient data. The definitions and some example calculations of the population systematic and random errors are given in the 'On Target' report (Section 4). These population measures are required for PTV margin determination.

10.14 ***Offline Imaging Strategy (systematic error correction)***

10.14.1 In an **offline** imaging strategy, images before treatment are acquired and a match to a reference image is made offline (i.e. without the patient on the couch). The purpose of the strategy is to reduce both the magnitude of the individual patient systematic set-up error, and when combined with other patients set up data treated under the same protocol, calculates the population systematic error. The population systematic error is the standard deviation of the systematic errors of all patients within the treated population.

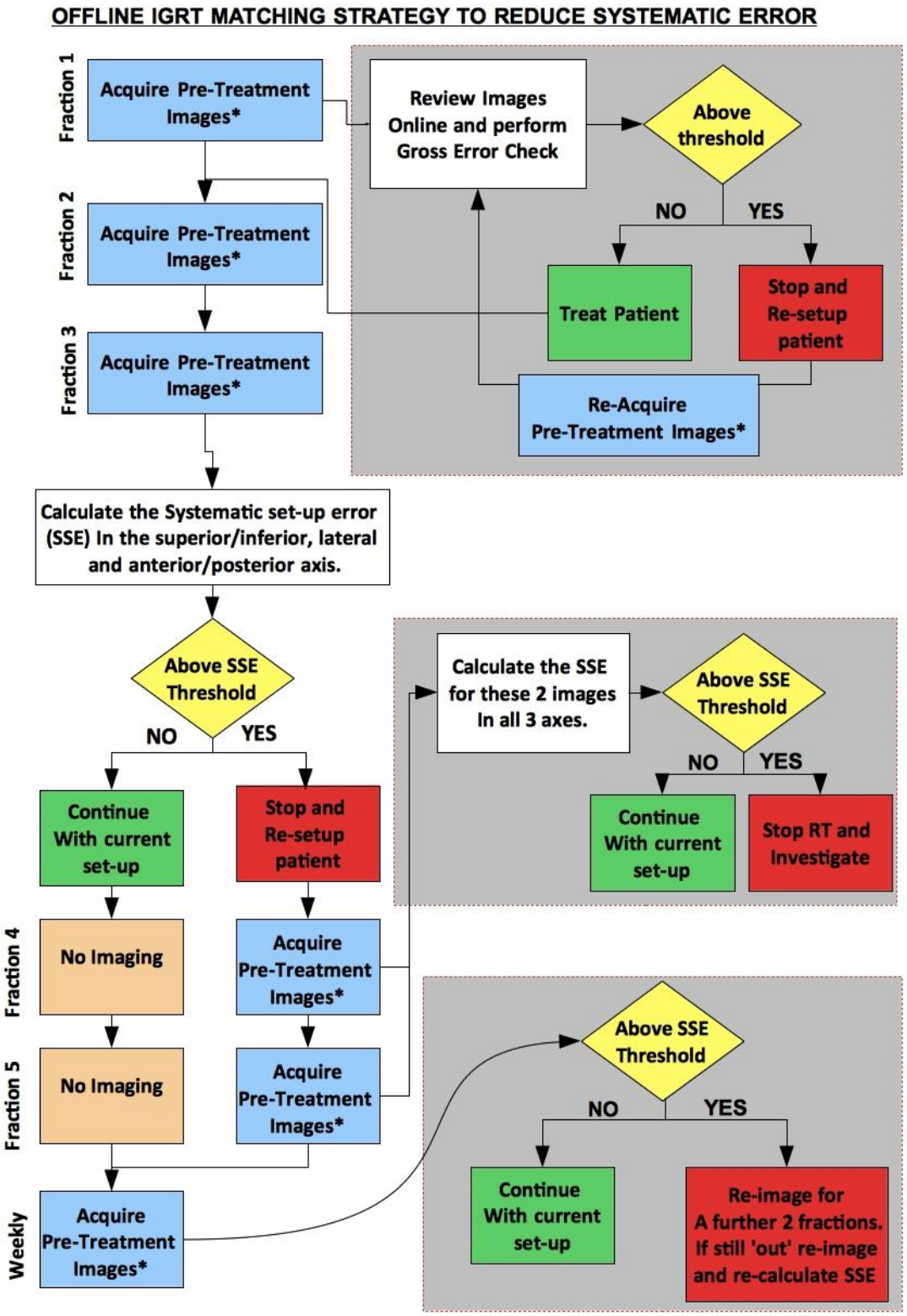
10.14.2 Published offline correction protocols which are widely used are the Shrinking Action Level (SAL)[8] and the No Action Level (NAL) protocols[9].

10.14.3 The SAL protocol uses an action level below which no correction is made; this action level changes with the number of measurements made. It may require up to 10 imaged fractions to halve the population systematic error with the SAL protocol.

10.14.4 The NAL protocol is simpler to apply as only one correction is made based on data from the first N imaged fractions. It is recommended that a minimum of 3 consecutive fractions are used to calculate the correction with a NAL protocol, as De Boer *et al*[9] found the use of 3 fractions data typically halved the population systematic error. The NAL protocol requires that all the calculated systematic error for each patient is corrected (there is no threshold for action).

10.14.5 Ideally all systematic errors should be corrected. However, if other correction protocols are used where thresholds are applied to the correction of patient systematic errors, the impact of the thresholds must be evaluated i.e. the post correction error distribution is evaluated, and the PTV margins should be derived accordingly. If not all the systematic error is

corrected there is a greater likelihood of any subsequent weekly check images being out of tolerance. If weekly, or more frequent, check imaging is carried out the data should be used to calculate an updated systematic error correction[10].




*can be volumetric or planar images

***Online Imaging Strategy (systematic and random correction)***

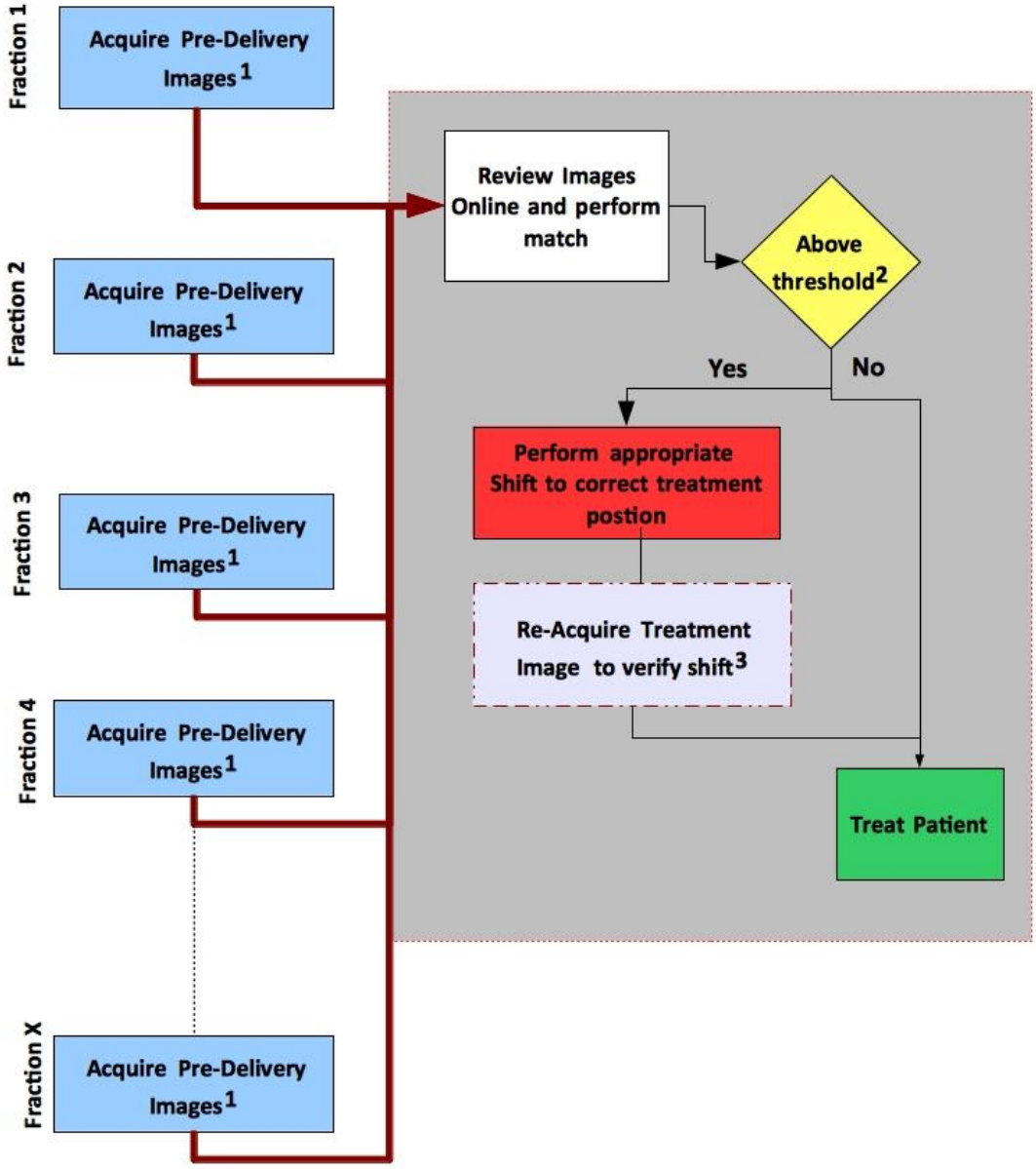
10.15.1 In an online imaging strategy images are acquired and then checked and corrected, prior to the day's treatment. The purpose of an **online imaging** strategy is to control and reduce both **systematic and random errors**.

10.15.2 With the widespread availability of automatic couch correction linked to imaging systems, there is no practical reason why the total measured displacement is not corrected each time online imaging and matching occurs. If a specified threshold or action level is used, below which no correction is made, the source, magnitude and impact of it should be justified for each treatment site (See Lam *et al* for one model), and the effect on the residual systematic error estimated for the population of patients and included in the PTV margin.

10.15.3 On line imaging can be performed for a limited number, or all radiotherapy fractions i.e. daily. If performed for a limited number of fractions it is essential to calculate the systematic error from the data and apply a correction for this to all other fractions. If thresholds are used for correction then their source, magnitude and impact should be determined and justified for each treatment site.

10.15.4 If imaging and correction occurs on every treatment fraction then the systematic and random errors may be calculated from the matched data . Post-treatment imaging would be required to quantify both intrafraction motion and residual errors. If evaluated for a patient population these data may be used to check the PTV margin for that treatment protocol.

## ONLINE IGRT MATCHING STRATEGY TO REDUCE SYSTEMATIC AND RANDOM ERROR




1 Can be volumetric or planar images

2 If thresholds are used then they should be justified and incorporated into treatment margins.

3 Only if required, e.g. for some SABR hypofractionated treatments or where verification of the couch shift is necessary

4 For some anatomical sites where the random error is typically small the imaging frequency can be reduced, i.e. not every fraction.

**Summary: I**n standard practice IGRT ensures that radiotherapy is targeted more accurately.

In addition IGRT has the potential to allow a reduction in the setup margin for a particular site that can:

- Facilitate dose escalation based on a margin reduction
- Reduce dose to normal tissue thereby reducing acute and late side effects

However, such reductions in set-up margin should be performed in the context of a clinical trial or prospective audit to ensure that outcomes are improved.

**References**


8 Bel A, van Herk M, Bartelink H, Lebesque JV. A verification procedure to improve patient set-up accuracy using portal images. Radiother Oncol. 1993 Nov;29(2):253-60. PubMed PMID: 8310153.

9 de Boer HC, van Os MJ, Jansen PP, Heijmen BJ. 17. Application of the No Action Level (NAL) protocol to correct for prostate motion based on electronic portal imaging of implanted markers. Int J Radiat Oncol Biol Phys. 2005 Mar 15;61(4):969-83.

10 de Boer HC, Heijmen BJ. eNAL: an extension of the NAL setup correction protocol for effective use of weekly follow-up measurements. Int J Radiat Oncol Biol Phys. 2007 Apr 1;67(5):1586-95. PubMed PMID: 17394953.

## 11.0 The IGRT Process

11.1 When establishing an IGRT service development strategy the entire process of IGRT (as described in this document) should be considered from radiotherapy planning and throughout treatment. The detail of the process is illustrated in appendix V. This may involve adaptive planning and verification as highlighted in red, but not when initially implementing the strategy.

## 12.0 Application of IGRT

12.1 The level of benefit in improving accuracy and precision in radiotherapy varies according to the tumour site being treated, and the specific needs of each patient.

12.2 The table below illustrates methods to increase radiotherapy precision. These can be combined to form different levels of complexity of IGRT, from its use in radiotherapy planning (level 0) through to treatment delivery (1-3) and treatment adaption (level 4). These levels are as a guide only, providing a common language for use and may change with technology development .

12.10 Guidelines for use for each tumour group are given later in this document.

12.11 When initially implementing the strategy it may be prudent to start with one site and level before progressing and expanding to other sites. As new techniques and technology become available the process must be reviewed to ensure quality is maintained and developments can be introduced. It may be useful to visit departments with the techniques/technology already in place.

## 13.0 Levels of IGRT complexity

| | Level | Goal | Imaging Technique | Imaging frequency | Correction strategy *(or comment)* |
|---|---|---|---|---|---|
| RT planning (for localisation of target volumes & OAR's) | **0a** | Reduce uncertainty in defining target | Planning CT | Once only | *Definition of Physical targets and Organs at Risk (OAR's)* |
| | **0b** | Reduce uncertainty in defining target | Planning CT + use of contrast agent | Once only | *Improves definition of physical targets and OAR's* |
| | **0c** | Reduce uncertainty in defining target | Planning CT + MRI or PET | Once only | *Improves definition of physical targets and OAR's and defines functional targets and OAR's* |
| | **0d** | Reduce uncertainty in defining target | 4D planning CT or multiple CT's prior to treatment to determine patient specific variations in anatomies | Once only (4DCT) or multiple CTs | *Physiological target and OAR's defined by combining GTV's from all phases or scans* |
| Treatment (comparing surrogate anatomy) | **1a** | Reduce gross setup error | Analyse using bony anatomy | First fraction only | Online: Correct gross error |
| | **1b** | Reduce initial systematic setup error | Analyse using bony anatomy | First 3-5 fractions and weekly | Offline: 1st 3-5 # Calculate and correct systematic error * Weekly- check within threshold |
| | **1c** | Continuous reduction of systematic error | Analyse using bony anatomy | First 3-5 fractions and weekly | Offline: 1st 3-5# Calculate and correct systematic error* Weekly- re-calculate and correct systematic error |
| | **1d** | Reduce random and systematic error | Analyse using bony anatomy | Daily or less | Online : if <daily then calculate and correct systematic errors* |
| | **1e** | Reduce uncertainty from anatomy changing trends | Analyse using bony anatomy and/or visual check/quantitative check of set up parameters | Weekly or more frequently | Off line: Consider intervention |

| | Level | Goal | Imaging Technique | Imaging frequency | Correction strategy *(or comment)* |
|---|---|---|---|---|---|
| Treatment (comparing target anatomy) | **2a** | Reduce gross setup error | Analyse using target anatomy or implanted markers | First fraction only | Online: Correct gross error |
| | **2b** | Reduce initial systematic error | Analyse using target anatomy or implanted markers | First 3-5 fractions and weekly | Offline: 1st 3-5# Calculate and correct Systematic error* Weekly- check within tolerance |
| | **2c** | Continuous reduction of systematic error | Analyse using target anatomy or implanted markers | First 3-5 fractions and weekly | Offline: 1st 3-5# Calculate and correct systematic error Weekly- re-calculate and correct systematic error |
| | **2d** | Reduce random and systematic error | Analyse using target anatomy or implanted markers | Daily | Online: daily imaging ideally throughout treatment course** |
| | **2e** | Reduce uncertainty from gross anatomy changes of target or OAR | Analyse using target anatomy or implanted markers | Weekly or more frequently | Online or offline: Consider intervention |
| Treatment (correct intrafractional error) | **3a** | Reduce intra-fraction errors | Online analysis using tracking (repeated imaging during delivery) | Real time or periodic intermittent imaging (can be in conj. with any other imaging freq.) | Online: Interrupt treatment during delivery and correct errors greater than action level |
| | **3b** | Reduce uncertainty from physiological movements (i.e. respiratory) | Online analysis using automatically gated imaging system (delivered only when target within treatable position) | Real time monitoring | Online: System automatically gated to deliver only when tumour is within treatable position (following action level). |
| | **3c** | Reduce uncertainty from physiological movements (i.e. respiratory) and automatically correct | Automatic online detection and analysis of target position | Real time monitoring | Online: System configured to change the treatment field to track the tumour. |

| | Level | Goal | Imaging Technique | Imaging frequency | Correction strategy *(or comment)* |
|---|---|---|---|---|---|
| Adaptive RT | 4a | Reduce uncertainties from shape change (pre-scheduled repeat planning CT) | Schedule repeat planning imaging during treatment course.<br>Offline dosimetric assessment | Once to weekly | Re-plan when dosimetric action level exceeded |
| | 4b | Reduce uncertainties from shape change | Treatment unit imaging & online or offline dosimetric analysis (identifying changes in probable tumour coverage from shape change) | As seen | Re-plan to assess for dosimetric changes. Implement changes |
| | 4c | Reduce uncertainties from shape change (pre-planned treatment imaging assessments) | Treatment unit imaging & online or offline geometric analysis<br>Compare plan database for best fit (for that fraction) | Each fraction | Deliver 'plan-of-the-day' for that fraction |
| | 4d | Reduce uncertainties from shape change (react throughout treatment imaging session) | Treatment unit imaging & online dosimetric analysis | Each fraction | Real-time (4D) ART |

*If thresholds are used for online correction or systematic error correction then these should be justified and incorporated into treatment margins

** For some treatment sites the random error is small and daily imaging with online correction may not be required. This increased uncertainty in the random error should be accounted for in the treatment margins

## 14.0 Local implementation of IGRT

14.1 The level of IGRT used will vary depending on anatomical site, delivery technique, and margins. Each department should consider training implications of each IGRT technique and develop training packages accordingly.

## 15.0 Training and responsibilities

15.1 IGRT is a core component of modern radiotherapy services and requires a multi-professional team approach and provides opportunities for expanded professional development. It is the responsibility of each therapeutic radiographer, medical physicist, dosimetrist and clinical oncologist (and all clinical practitioners) to ensure that they maintain their skills as technology evolves. Employers should also ensure that staff involved in IGRT based on the principles in this document acquire and maintain the necessary skills. Competency for all clinical disciplines should be regularly assessed against current clinical standards which the professional bodies, i.e. RCR, SCoR and IPEM, should consider defining. In order for IGRT strategies to be implemented, efficient and confident acquisition and assessment of the verification images is required. However imaging technology in radiotherapy has increased in complexity and amount of information over the last 10 years and it is essential that post graduate and undergraduate training and assessments reflect these changes.

15.2 Roles and responsibilities will continue to change to meet the needs of implementing IGRT techniques and training requirements in each centre will depend on:

- Number of IGRT capable linear accelerators
- Number of therapeutic radiographers
- Length of time therapeutic radiographers will spend on IGRT linac
- Number of anatomical sites where IGRT will be used

15.3 **Levels of training**

**1. Core Skills**

Each of the professional disciplines should ensure that they have skills and competencies in:

- implementation process
- developing site specific protocols
- off-protocol decision making
- review of images (in conjunction with other disciplines)
- assessment for re-plan
- audit re-plan rate
- Manufacturer application training and/or cascade training for all disciplines.

- Local IGRT protocol knowledge and understanding

Specifically each discipline will require appropriate training i.e.

- Clinical Oncologist – image interpretation including impact of changes on target coverage and OAR doses
- Therapeutic radiographer – image acquisition, image registration, image interpretation
- Physicist - image interpretation, methods of improving image quality, image transfer to TPS and image quality assurance.

In addition every department should have at least one IGRT specialist with responsibility for ensuring that the appropriate application of IGRT across a service, i.e. a dedicated **IGRT specialist therapeutic radiographer.**

The IGRT specialist therapeutic radiographer:

- needs to undertake a recognised IGRT training program for example ESTRO IGRT course, MSc module etc.
- have in-depth knowledge of the types of geometric errors that can occur in radiotherapy practice, methods that can be used to minimise them and appropriate directional tolerances for complex treatments
- should regularly interact with other IGRT specialists outside their service to ensure a wide scope of knowledge is maintained.
- be clinically competent in the regular delivery of IGRT and have the ability to cascade this knowledge.
- should have competency and the authority to sign off training in other users.

Any member of the clinical team can be an IGRT user but the level depends on the task required and whether the individual has the appropriate training and skills. For the purpose of this document we have defined this as regular and advanced users.

**2. Regular IGRT user training**

- Image acquisition with planar and/or volumetric imaging.
- Image interpretation of bony anatomy, and surrogate targets
- Be able to identify gross changes in patient's anatomy
- Understanding of systematic and random error reduction strategies.

**3. Advanced IGRT user training**

- Competent in soft tissue matching for standard fractionated radiotherapy protocols
- Online decision making for hypofractionated treatments including deciding the threshold to seek physicist and oncology input.

15.4 Each discipline will require different levels of training for their role in the image review process.

15.5 It may be useful for individual departments to consider the use of different levels of training depending on their case mix and IGRT requirements.

## 16.0 Implementation programme

16.1 It is recognised that manufacturer training is essential to get started. This training will cover practical aspects associated with utilisation of the equipment and include hardware and software capabilities. All disciplines should attend this training, where possible.

16.2 Prior to clinical use, users should become familiar with the system by using anatomical phantoms. This can be incorporated into the commissioning/acceptance process (image quality is discussed in more detail later in this document).

16.3 Prior to implementing image guidance techniques, it is imperative that each department establish an IGRT implementation team comprising a lead IGRT physicist, therapeutic radiographer, and clinical oncologist. This team may be site-specific but if general, a site-specific clinical oncologist must be an additional member of the team. The implementation team should visit other centres (at least one) with the same equipment and where IGRT has been implemented across a range of anatomical sites.

16.4 It is recommended to concentrate on one anatomical site initially, considering the patient population and evidence for IGRT in this document. Set-up data should be collected based on conventional bone match approaches before moving on to soft tissue evaluation. Following this, the optimal protocol for each anatomical site can be determined. For example, tolerances, action levels, who will be reviewing the images and when the images are to be reviewed, i.e. whether this will be online or offline protocols. The use of risk assessments for each IGRT technique, is recommended (see appendix VI)

16.5 We would envisage that the IGRT specialist therapeutic radiographer would be the appropriate trainer for the majority of IGRT education. However, for certain tasks, e.g. image quality assurance, another member of the implementation team may do the training.

16.6 The IGRT specialist therapeutic radiographer with the IGRT implementation team would also develop an education programme for training therapeutic radiographers (an example is detailed in appendix VII). The IGRT implementation team should collectively approve the level of skills and knowledge needed for the specific IGRT application and the trainer then can assesses each staff for competency against the levels set.

16.7 When reviewing images it is important to have knowledge of the patient set-up at the time of image acquisition. Therapeutic radiographers are therefore best placed to review and analyse the images and set-up. Image review then becomes an integral part of the treatment

process and any therapeutic radiographer deemed to be competent ought to be able to carry out this task.

16.8 The following components of the IGRT process should be considered when devising an IGRT implementation programme.

1. Acquisition – choosing the most appropriate imaging technique for the site treated and/or technique used.
2. Analysis – understanding and awareness of the tools available on the IGRT system. For example, consider ambient lighting, the use of windowing and how the system compensates for rotational errors.
3. Action Levels which should be based on
    - the clinical protocol for that site
    - organs at risk (interpretation of DVH's maybe required)
    - changes in external/internal anatomy
    - information from clinician / planner to person reviewing the image

16.9 In addition we recommend:

- Weekly review of images by clinician– especially when starting IGRT for new sites for training and analysis.
- A regular audit of the therapeutic radiographers' image review decision making by taking random samples of patient image data and verifying that the correct decision had been made.
- Processes to be actioned when significant changes are observed. The team developing the technique should detail the level of significant change and action levels; this could include dosimetric analysis and re-planning. This will require departmental guidelines and appropriate training.
- An audit of the re-plan rate. This falls in the remit of the IGRT implementation team.

## 17.0 Image Quality

17.1 The aim of these guidelines is not to provide detailed guidance on methods for ensuring optimal image quality, as this will differ based on the RT centre's equipment, staff and clinical protocols. Technical recommendations for measuring, optimising and maintaining image quality will be provided by the report of the IPEM IGRT Working Party, due to be published summer/ autumn 2012.

17.2 However, there are over-arching principles regarding image quality and optimisation that are discussed below. A 'good quality' image is one that is suitable for the clinical task and may not be the best possible image attainable. Importantly, a good quality image for one task may be not be appropriate for another. The optimal image is one where all competing factors have been balanced to achieve an image of appropriate quality with the least burden to the patient and clinical service. For ionising radiation this generally entails a trade-off between patient dose and image quality, though the cost of equipment and patient throughput are factors which may need to be considered. There is always a trade off between the increased time and/or dose required to achieve a high quality image and the patient maintaining a consistent position during the radiotherapy fraction. For the IGRT clinical task the concept of 'image quality' covers both geometric accuracy and the ability to interpret and act appropriately on that image.

17.3 The aim of IGRT is to produce an image with a dose that is **a**s **l**ow **a**s **r**easonably **a**chievable (ALARA) yet still be of adequate quality to perform the task. Under IR(ME)R the optimisation process should closely involve a Medical Physics Expert (MPE) and it is essential that the MPE works as part of the clinical team. 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. For example, the additional dose required for a 4DCT planning scan can be justified if it produces better quality CT images of moving targets and allows more accurate measurement of target motion.

17.4 It is important that the doses associated with different imaging protocols are characterised and that the influence on dose and image quality of changing acquisition settings for individual patients is understood. Centres are encouraged to establish local dose reference levels which can be compared against and which should be actively monitored over time. Whilst not a requirement under IR(ME)R, as it is for diagnostic imaging, this is regarded as good practice. Furthermore, centres with similar imaging equipment and patient workloads are encouraged to compare doses against each other. In addition, centres are strongly encouraged to participate in regional and national audit programmes, such as that led by the IPEM Inter-departmental Dosimetry Audit.

17.5 The quality and reconstruction of the initial planning CT scan will influence the accuracy of the IGRT matching process on treatment. A balance is required to ensure the quality of the planning scan is sufficient for all the applications to which it is being applied. For example, the quality of digitally reconstructed radiographs (DRRs) is fundamentally linked to CT slice thickness, with DRR spatial resolution (and therefore potential accuracy of matching)

improving as CT slice thickness is decreased. However, thinner slices at a particular dose level yield a greater number and nosier images and may be more difficult to outline. When developing an IGRT strategy it is important to learn from established techniques already available and used in diagnostic imaging. For example, a possible solution is to scan at a thin slice thickness then reconstructing at a thicker one, with the thin slices being used for image matching during treatment and the thicker slices being used to characterise the target volume.

17.6 Through optimising image quality the aim is to ensure:

- images acquired and presented are consistently of sufficient quality for the clinical task
- that the dose burden does not change over time
- the consistency of image quality
- the consistent performance of the clinical task by trained operators

17.7 There are recognised measurement techniques that are based on established practice in both the diagnostic and radiotherapy communities. However, these are not always consistent between modalities or communities. In order to optimise across the radiotherapy process it is important to standardise across all modalities and employ a common language. If local QA procedures differ from standard methods then this should be understood and traceability to a standard approach should exist.

17.8 There should be awareness of common image artefacts, their causes, workarounds or avoidance methods and their impact on the clinical task.

17.9 Measurements can be qualitative, semi-quantitative and quantitative. Quantitative measurements are preferred because these give numerical results which are independent of the operator, can be compared against those from other centres, be utilised directly in optimisation exercises and used to track trends over time.

17.10 The same equipment (e.g. phantoms) should be used for measurements on both planning imaging and linac based imaging.

17.11 Clinical staff should be involved in any QA programme to ensure that they are aware of their system's performance and tolerance limits

17.12 Display devices (e.g. monitors) must be considered alongside the image acquisition equipment as geometrical errors can result if these are not performing as intended.

17.13 As new IGRT imaging equipment becomes available and the sophistication of imaging procedures increases it is important to keep abreast of newer national and international guidance. 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. However, a full characterisation of new imaging facilities during the clinical commissioning process requires substantial effort that may be better invested in bringing the new equipment into clinical use. It is therefore strongly encouraged that centres

with similar equipment build on each other's expertise. Imaging protocols and QA procedures should be regularly reviewed to ensure they remain fit for purpose. Ongoing access for physics measurement will be required for this.

## 18.0 Data Collection

18.1 Data collection is one of the most critical aspects to ensure the safe implementation and use of IGRT. It is important to verify and check set-up **margins,** is imperative to minimise the **dose** used for IGRT (whilst still providing sufficient image quality to perform the IGRT task), and key for **activity recording**.

18.2 **Margins:** IGRT can be used to check current practice, and if done prospectively can be used to evaluate new methods of RT delivery including IMRT, SABR and margin reduction. However, collecting these IGRT data and using it can have significant impact on a radiotherapy department resources.

18.3 As demonstrated by an online survey (appendix IV) performed by the NRIG IGRT group the "On Target" recommendations are still not universally implemented.

18.4 Therefore, it is critical for each centre to audit their individual practice and part of routine audit and service development. Ideally all set-up data for an individual patient, individual linear accelerator and tumour sites across the department should be prospectively collected. In the ideal scenario this data would automatically calculate the patient's systematic +/- random error and populate the tumour site data to generate institutional margins.

18.5 However, this is currently not available in most centres and therefore we recommend that for each common tumour site a centre should audit the set-up data for at least 20 patients. Using the method identified on the National Cancer Action Team website (www.ncat.nhs.uk/radiotherapy), the service should calculate their own setup margins. This should be repeated every 1-2 years or if there is a change in the RT process e.g. new immobilisation, new radiotherapy technique or new linear accelerators.

18.6 **Dose:** A requirement of IR(ME)R is to record factors relevant to patient dose. In the online survey ≈40% of centres' clinical protocols include typical imaging dose value per exposure and only half of the centres had clinical protocols that included imaging dose limits.

18.7 The document "A guide to understanding the Implications of the Ionising Radiation (Medical Exposure) Regulations in Radiotherapy" (RCR 2008) addresses the justification of verification images involving additional radiation. Interpretation for concomitant exposures is that a record should be kept of the exposure factors and volume parameters, which affect radiation dose.

18.8 In the context of IGRT imaging systems, the requirements on Quality Control should be applied in a similar way to that required for diagnostic X-ray systems regulation. In particular, technical procedures are established, in which the dose necessary for imaging is documented or an estimate of this dose made by the user.

18.9 The exposure factors recorded will differ between imaging modalities and vendor systems hence it is difficult to set definitive limits and advise on a national guidance.

18.10 It is good practice to calculate a dose estimate (single dose figure on central axis) for each concomitant exposure. Clinical protocols should include typical imaging dose values per exposure and state imaging dose limits for a complete treatment course (or a typical maximum number of images on each system (MV portals , kV CBCT, etc).

18.11 Individual clinical trial protocols should state a minimum accepted level of IGRT for the trial. This level, for some trials, may be higher than is routinely used at a centre. The protocol IGRT specifications should also provide recommendations on estimating patient dose due to the IGRT component of the study. Clinical trial participation is encouraged to implement IGRT protocols safely and efficiently.

18.12 **Activity recording:** From 1st April 2009, All Radiotherapy Services have been required to return the Radiotherapy Dataset (RTDS) data to the National Cancer Services Analysis Team (NATCANSAT) for all external beam and brachytherapy activity. This has allowed the routine collection of clinically and managerially relevant activity data from Radiotherapy facilities in order to commission or monitor RT services in an evidence-based manner.

18.13 These data extracts include all radiotherapy attendance records including the relevant OPCS4 code per fraction treated. The coding structure unfortunately only allows a limited clinical, managerial or commissioning review of the extent of IGRT being undertaken due to a limited range of available codes. There are only 3 codes available to be attributed to a fraction of external beam radiotherapy.

- Y91.1. **Complex** which includes delivery that involves significant serial imaging for systematic errors. Clearly this does not quantify for how many fractions imaging is actually undertaken.
- Y91.2. **Simple** which includes any other simple techniques that do not require serial imaging.
- Y91.4. **Adaptive** which does clearly indicate that that particular fraction included production of a three-dimensional image (e.g. cone-beam CT, ultrasound or the use of fiducial markers) so that the field position may be changed at the time of treatment if necessary.

18.14 In addition to this limited range of available codes to enable a direct review of quality and quantity of imaging, there is also a perceived lack of coding accuracy within certain centres. For example it has been seen in analyses of the RTDS data that known centres with a high proportion of on-line 3D cone beam CT IGRT are not using the Y91.4 code appropriately, if at all. It is therefore recommended that each centre ensures absolute compliance with the nationally available coding guidance and in addition that the National Radiotherapy Implementation Group continues to influence the development of OPCS codes such that they continue to reflect developing practice.

## 19.0 Trials and Future Use

19.1 **Trials:** As more complex and sophisticated planning and delivery techniques are being employed in clinical trials, an IGRT component is becoming a standard inclusion in trial protocols.

19.2 **Two main scenarios for IGRT use in clinical trials:**

a. Trials testing/comparing one IGRT method over another.

Such trials are unlikely to be performed on a National scale as IGRT is a tool rather than a treatment technique. However such studies should be done on a local level to ascertain how different approaches should best be used.

b. Trials using complex RT techniques

These may fall into one, or more of the following categories:

(i) Evaluation of IGRT technique

(ii) Trial requires a specific accuracy in verification

(iii) Trial requires implementation of an IGRT technique that is new to an investigator site.

19.3 In the UK notable IGRT sub-studies have been associated with Phase III randomised trials.

a) CHHiP IGRT sub-study (ISRCTN 97182923) to assess the acute and late toxicity associated with IGRT (standard margins vs. reduced margins) and to determine feasibility of a phase III randomised trial of IGRT in the treatment of localised prostate cancer.

b) IMPORT HIGH IGRT sub-study (ISRCTN 47437448) comparing the positional accuracy of breast radiotherapy based on imaging; (i) titanium markers implanted in the tumour bed (IGRT) and (ii) bony anatomy and lung position (standard imaging) during curative radiotherapy for early breast cancer.

19.4 Clinical trial protocols should provide instructions and guidelines on method(s) of IGRT permitted for the trial and the correction strategy to be used with suggested tolerances.

19.5 IGRT QA is challenging when both vendor equipment and imaging modality may vary across multiple investigator sites introducing uncertainties. A comprehensive QA programme should be in place to recommend minimum IGRT requirements for all trials[11]. For some trials, centres may be required to complete an IGRT credentialing programme prior to patient recruitment, such as a modular programme, similar to that implemented by the NCRI RTTQA group to credential centres for use of IMRT in clinical trials.

19.6 Components of an IGRT QA programme:

- Questionnaire-IGRT generic and trial specific

- Process document-Details of all aspects of the tasks for a complete patient pathway to include details on all imaging procedures
- Verification of electronic data transfer DICOM data transfer check to and from investigator site. Confirmation that transferred data is anonymous
- Image quality assessment -To ensure consistency of image quality and suitability of image for the clinical task
- Image dose assessment -Documentation of dose resulting from imaging procedure
- Image registration evaluation-Independent software evaluation of registration accuracy to (a) ensure registration accuracy for different imaging modalities is consistent with reported data (b) ensure that the person performing the registration is competent and appropriately trained to do so.
- Site visit (QA tests for system accuracy, real time review of registration)

19.7 Completion of all modules would be required for the first complex IGRT trial and on successful completion the centre would be considered IGRT credentialed. For subsequent trials the IGRT QA burden could be reduced appropriately, depending on anatomical site and trial complexity. This process will be influenced by equipment changes and upgrades.

## 20.0 FUTURE USE

20.1 Standard treatment delivery uses population based margins to compensate for treatment delivery errors but in an era where hypofractionation and stereotactic treatments are increasingly used the need for on-line daily imaging and correction prior to treatment delivery is increasing.

20.2 Where targets are both mobile and deformable, treatments need to be more complex and may involve the following:

- the use of a composite plan which either uses a number of pre-treatment images and/or off-line assessments to measure the average systematic and random error for each individual patient[12,13].
- the use of a 'plan of the day' strategy where daily on-line volumetric imaging is used to select the plan that best covers the target from a library of plans[14].

20.3 To date the clinical trial experience of complex treatment is limited to single centre experiences. Planning with a 'plan of the day' approach appears most promising with bladder radiotherapy as this is a target subject to large random changes in volume which are generally easily identified using on-treatment volumetric imaging[15].

20.4 4D adaptive radiotherapy can also involve dosimetric evaluation of actual delivered doses to both the target and organs at risk. In head and neck radiotherapy there are significant changes in anatomy over the course of treatment delivery. Although not usually subject to significant organ motion, changes in anatomy are seen due to tumour shrinkage, tissue oedema and weight loss. Technologies such as TomoTherapy incorporate planning systems that can give cumulative dose statistics through treatment delivery. Initial studies demonstrate that in Head and Neck radiotherapy the dose delivered to critical structures can be significantly different to that planned[16]. Work is on-going to try and identify criteria that can be used to identify those patients that may benefit from an on-going dosimetric evaluation during treatment delivery.

**References:**


11 Image Guided Radiation Therapy Guidelines: ATC QA subcommittee report, October 18, 2009

12 Brabbins D, Martinez A, Yan D, Lockman D, Wallace M, Gustafson G, Chen P, Vicini F, Wong J. A dose-escalation trial with the adaptive radiotherapy process as a delivery system in localized prostate cancer: analysis of chronic toxicity. Int J Radiat Oncol Biol Phys. 2005 Feb 1;61(2):400-8. PubMed PMID: 15667959.

13 Pos FJ, Hulshof M, Lebesque J, Lotz H, van Tienhoven G, Moonen L, Remeijer P. Adaptive radiotherapy for invasive bladder cancer: a feasibility study. Int J Radiat Oncol Biol Phys. 2006 Mar 1;64(3):862-8. PubMed PMID: 16458776.

14 Burridge N, Amer A, Marchant T, et al. Online adaptive radiotherapy of the bladder: small bowel irradiated-volume reduction. Int J Radiat Oncol Biol Phys 2006;66(3):892-897.

15 Lalondrelle S, Huddart R. Improving radiotherapy for bladder cancer: an opportunity to integrate new technologies. Clin Oncol (R Coll Radiol). 2009 Jun;21(5):380-4. Epub 2009 Apr 25. PubMed PMID: 19394804.

16 Castadot P, Geets X, Lee JA, Grégoire V. Adaptive functional image-guided IMRT in pharyngo-laryngeal squamous cell carcinoma: is the gain in dose distribution worth the effort? Radiother Oncol. 2011 Dec;101(3):343-50. Epub 2011 Jul 1.PubMed PMID: 21724283.

## 21.0 Integration of functional imaging to guide treatment

21.1 CT has excellent spatial reproducibility and currently is the backbone of 3D conformal radiotherapy planning. Unfortunately CT does not always offer adequate soft tissue contrast or information regarding function, oxygenation, proliferation etc. This has resulted in incorporation of other imaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography (PET) for target volumes definition through the process of image registration. PET is the most studied technology, but the best method to incorporate functional PET data into RT planning is still a matter of debate.

- The ability to spatially measure biological or metabolic processes with imaging may enable modification of radiation delivery to account for an individual's variability in tumour biology in a spatial and time-responsive manner[17].This has led to the development of two concepts:
    - modifying radiotherapy using the incorporation of temporal modification of tumour biology
    - the concept of physical dose variation according to certain characteristics of the molecular imaging.

21.2 Current trends for incorporating PET imaging in treatment planning:

- Use of PET to define GTV in addition to CT using a predefined segmentation algorithm. This technique has been applied in several tumour sites such as: head and neck cancers[18], brain[19], lung cancer[20].
- Use PET information to define a sub-volume in a CT derived GTV[21]. This volume would then receive a higher dose of RT and it is referred to as dose painting by contours[22].
- The functional PET image can be used to define the dose according to the voxel intensities[23,24]. This concept is known as dose painting by numbers. This is currently being tested in head and neck cancers[25,26].

21.3 The practical implementation of PET for radiotherapy planning and plan modification during radiotherapy is currently subjected to a large number of limitations and uncertainties. Accurate positioning and immobilization for PET as for RT planning must be achieved[27] accuracy of target delineation is directly conditioned by the image quality and delineations algorithms[28]. Respiratory gated PET need to be considered if there is significant target motion[29]. A significant number of these techniques have not been validated, but there is early clinical data for use in several tumour sites available[30,31].

21.4 For all tumour sites, PET cannot yet be routinely incorporated in the treatment planning process, as better understanding of tumour and normal tissue biology and further characterization of the radiopharmaceutical used is needed.

## 22.0 IGRT Emerging Technologies

22.1 Current technologies are continuously improving. In IGRT using kV X-rays, manufacturers and their clinical collaborators are working on improving image quality, reducing risks and patient dose, improving speed and efficiency of use. Examples include kV cone-beam during first arc of VMAT delivery ready to re-evaluate patient setup prior to second arc, and 2D imaging with marker registration (using 'on-board kV') during treatment delivery.

22.2 Other developments in IGRT technology include compact MV imaging with CT on a bespoke gantry ring, CT on rails and MR-linac combinations[32,33].The advantage of MRI at the linac being the addition soft-tissue form as well as functional imaging capability, although work is needed to address the effects the magnetic field in the room will have on the beam. Further developments such as the combined PET-MRI scanner[34] will allow a range of functional images to guide the clinical team in targeting as well as determining the correct dose for the correct part of the tumour. The question remains whether this technology could also be installed into the treatment room.

22.3 The technologies which are currently emerging are addressing the issues of providing imaging information on form and function as well as providing the capability to carry out IGRT on-line. In future adaptive IGRT, with on-line changes made to the plan as well as the set-up of the patient, will replace the current workflow where set-up is corrected but the plan is maintained and adaptive radiotherapy at the treatment machine will become the gold standard. Real time adaption of the plan to the current patient anatomy requires methods of deformable image registration, image segmentation, plan re-optimisation and dose calculation and dose summation/accumulation. Development of in-vivo portal dosimetry techniques will help facilitate this. Recently, progress has been made to improve workflows and techniques, which in time will make adaptive IGRT achievable in an accurate, robust and fully automated manner. However, there is still much work if this is to be implemented safely into clinical practice.

22.4 There will also be radically different couch designs[35]. These could allow repositioning of the patient without relocating the patient relative to the couch, however safety and patient comfort may limit their use.

22.5 Furthermore there will be novel ways to assess the position and shape of the patient with techniques such as optical surface sensing[36] and 'GPS for the body' using technologies such as miniature implanted transponders[37] to provide continuous information on the location of the tumour during irradiation.

22.6 The key issues for all of these technologies will be whether the imaging systems and processes are efficient and accurate enough.

**References:**


17. Thorwarth D, Geets X, Paiusco M. Physical radiotherapy treatment planning based on functional PET/CT data. Radiother Oncol. 2010 Sep;96(3):317-24. Epub 2010 Jul 30. Review. PubMed PMID: 20673689.

18. Geets X, Daisne JF, Tomsej M, Duprez T, Lonneux M, Grégoire V. Impact of the type of imaging modality on target volumes delineation and dose distribution in pharyngo-laryngeal squamous cell carcinoma: comparison between pre- and per-treatment studies. Radiother Oncol. 2006 Mar;78(3):291-7. Epub 2006 Feb 24. PubMed PMID: 16499982.

19. Douglas JG, Stelzer KJ, Mankoff DA, Tralins KS, Krohn KA, Muzi M, Silbergeld DL, Rostomily RC, Scharnhorst J, Spence AM. [F-18]-fluorodeoxyglucose positron emission tomography for targeting radiation dose escalation for patients with glioblastoma multiforme: clinical outcomes and patterns of failure. Int J Radiat Oncol Biol Phys. 2006 Mar 1;64(3):886-91. Epub 2005 Oct 19. PubMed PMID:16242251.

20. De Ruysscher D, Nestle U, Jeraj R, Macmanus M. PET scans in radiotherapy planning of lung cancer. Lung Cancer. 2012 Feb;75(2):141-5. Epub 2011 Sep 15. PubMed PMID: 21920625.

21. Ling CC, Humm J, Larson S, Amols H, Fuks Z, Leibel S, Koutcher JA. Towards multidimensional radiotherapy (MD-CRT): biological imaging and biological conformality. Int J Radiat Oncol Biol Phys. 2000 Jun 1;47(3):551-60. Review. PubMed PMID: 10837935.

22. Meijer G, Steenhuijsen J, Bal M, De Jaeger K, Schuring D, Theuws J. Dose painting by contours versus dose painting by numbers for stage II/III lung cancer: practical implications of using a broad or sharp brush. Radiother Oncol. 2011 Sep;100(3):396-401. Epub 2011 Sep 28. PubMed PMID: 21955663.

23. Bentzen SM. Theragnostic imaging for radiation oncology: dose-painting by numbers. Lancet Oncol. 2005 Feb;6(2):112-7. PubMed PMID: 15683820.

24. Alber M, Paulsen F, Eschmann SM, Machulla HJ. On biologically conformal boost dose optimization. Phys Med Biol. 2003 Jan 21;48(2):N31-5. PubMed PMID: 12587912.

25. Duprez F, De Neve W, De Gersem W, Coghe M, Madani I. Adaptive dose painting by numbers for head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2011 Jul 15;80(4):1045-55. Epub 2010 Jul 17. PubMed PMID: 20643512.

26. Madani I, Duprez F, Boterberg T, Van de Wiele C, Bonte K, Deron P, De Gersem W, Coghe M, De Neve W. Maximum tolerated dose in a phase I trial on adaptive dose painting by numbers for head and neck cancer. Radiother Oncol. 2011 Dec;101(3):351-5. PubMed PMID: 21742392.

27. Coffey M, Vaandering A. Patient setup for PET/CT acquisition in planning. Radiother Oncol. 2010 Sep;96(3):298-301. Epub 2010 Aug 18. Review. PubMed PMID: 20727605.

28. Lee JA. Segmentation of positron emission tomography images: some recommendations for target delineation in radiation oncology. Radiother Oncol. 2010 Sep;96(3):302-7. Epub 2010 Aug 11. Review. PubMed PMID: 20708286.

29. Bettinardi V, Picchio M, Di Muzio N, Gianolli L, Gilardi MC, Messa C. Detection and compensation of organ/lesion motion using 4D-PET/CT respiratory gated acquisition techniques. Radiother Oncol. 2010 Sep;96(3):311-6. Epub 2010 Aug 12. Review. PubMed PMID: 20708809.

30. Grosu AL, Weber WA. PET for radiation treatment planning of brain tumours. Radiother Oncol. 2010 Sep;96(3):325-7. Epub 2010 Aug 20. Review. PubMed PMID:20728952.

31. Lambrecht M, Haustermans K. Clinical evidence on PET-CT for radiation therapy planning in gastro-intestinal tumors. Radiother Oncol. 2010 Sep;96(3):339-46. Epub 2010 Aug 18. Review. PubMed PMID: 20727606.

32. Raaymakers BW, de Boer JC, Knox C, Crijns SP, Smit K, Stam MK, Bosch MR, Kok JG, Lagendijk JJ. Integrated megavoltage portal imaging with a 1.5 T MRI linac. Phys Med Biol. 2011 Oct 7;56(19):N207-14. Epub 2011 Sep 20. PubMed PMID:21934191.

33. Varian at Princess Margaret, Toronto, personal correspondence

34. Addenbrookes, Cavendish Centre, personal correspondence

35. Gevaert T, Verellen D, Engels B, Depuydt T, Heuninckx K, Tournel K, Duchateau M, Reynders T, De Ridder M. Clinical Evaluation of a Robotic 6-Degree of Freedom Treatment Couch for Frameless Radiosurgery. Int J Radiat Oncol Biol Phys. 2011 Sep 22. [Epub ahead of print] PubMed PMID: 21945110.

36. Price GJ, Parkhurst JM, Sharrock PJ, Moore CJ. Real-time optical measurement of the dynamic body surface for use in guided radiotherapy. Phys Med Biol. 2012 Jan 21;57(2):415-36.

37. Fast MF, Krauss A, Oelfke U, Nill S. Positional detection accuracy of a novel linac-mounted intrafractional x-ray imaging system. Med Phys. 2012 Jan;39(1):109

## 23.0 Indication of overall numbers / estimates of demand.

23.1 Every single patient should have a form of IGRT as part of their radiotherapy treatment. The frequency and complexity reflects the treatment intent, anatomical site and fractionation (as detailed in the site specific protocols).

23.2 Therefore, each individual service should make an estimate of demand based on their case mix and agreed local protocols.

23.3 Every service should take into account their existing IGRT capability and prioritise sites to maximise the clinical benefit gained according to the site specific protocols.

23.4 Every service needs to account for the needs for all patients to have access to appropriate IGRT and the limitations of their current prioritisation decisions to inform future choice of new equipment.

23.5 IGRT is the standard of care that we expect for all patients and more accurate treatment must be clinically beneficial. It is recognised that this is an additional step in the pathway and will therefore add time to the radiotherapy delivery.

23.6 Evidence from implementation of IMRT clearly demonstrates that through gaining experience, increasing patient numbers and improved delivery technology, the time required decreases.

23.7 For IGRT evidence suggests that the efficiency gains seen in IMRT will apply to IGRT.

23.8 IGRT can also facilitate hypofractionation (e.g. SABR), reducing total linac time.

23.9 It is the responsibility of service leaders and clinicians to maximise the efficiencies in these pathways.

## 24.0 National Implementation Strategy

24.1 Delivering an appropriate IGRT service requires that all providers are appropriately trained, use high quality protocols and apply the IGRT principles in a standard way.

24.2 Nationally NRIG will lead on early development and supporting local provision. However, it is important that this is in conjunction with a locally sustainable action plan.

24.3 NRIG therefore proposes the use of clinical champions employed by the National Cancer Action Team to provide on-site support in the writing of protocols, training in use of techniques and technology and in image matching and review. These national posts will support the development of local clinical champions, including the IGRT specialist therapeutic radiographer, who will support the development and implementation of IGRT in their centre.

24.4 It is intended to begin this process in Summer 2012. NRIG and the National Cancer Action Team will oversee this process.

24.5 Each NHS Radiotherapy service in England will be offered the support from clinical specialists in IGRT (both radiographic and scientific) during 2012/13. This team will visit services and provide training and support within the host environment tailored to a specific need.

24.6 This is designed to be a short-term approach, and locally, the creation of internal IGRT clinical champions within services will be necessary to maintain sustainability.

## 25.0 Credentialing

25.1 The challenges of IGRT QA are plentiful: different vendor's equipment, various imaging modalities, inter user variance, as well as variations in image quality, imaging frequency, tolerances and action levels. Robust IGRT QA is required in particular when considering dose escalation and hypofractionation.

25.2 A comprehensive credentialing programme serves to ensure proper implementation of IGRT in all institutions. Such a programme can be used to*:*

1) Benchmark against national and international standards
2) Standardise training and audit
3) Accredit centres for recruitment into clinical trials

## 26.0 Tariff and costs.

26.1 Services are remunerated by OPCS codes collected in HRGs. IGRT is recognised as adaptive radiotherapy within this structure. This does not reflect the varying levels of complexity in the IGRT process, i.e. simple planar bony match compared with multiple volumetric images during a single fraction (e.g. SABR).

26.2 In the interim we would encourage services to collect data on their current and future IGRT use to aid future dialogue with commissioners.

## 27.0 Conclusions and recommendations for future use.

27.1 IGRT should be used for every radiotherapy episode according that patient's needs based upon these guidelines and according to a locally developed protocol.

27.2 Every centre should have an IGRT multi-disciplinary team that includes at least one IGRT specialist therapeutic radiographer.

27.3 In the next 12 months services should move to the routine use of IGRT based upon the principles detailed in 'On-Target' and then built upon in this report. This should be supported by an on going service development strategy for more complex IGRT methods in the future.

27.4 To fulfil the IGRT site-specific guidelines as detailed in this document, consideration on the appropriate configuration of new radiotherapy equipment should be made as part of the procurement strategy.

27.5 The additional dose involved in IGRT should be recorded, monitored and justified in the local site specific protocols (ALARA).

27.6 Routine prospective IGRT data collection for the individual patient and individual anatomical sites in a radiotherapy department is essential to calculate the systematic and random errors and inform local margins.

27.7 Although image review is a core skill of all clinical staff it should be performed by the individuals involved in the treatment delivery of the patient imaged. The ability should be assessed by peer and self assessed competencies

27.8 Effective immobilisation is essential to ensure the patient remains in a reproducible and consistent position through out the radiotherapy pathway and during the treatment delivery and verification process.

27.9 Centres should be encouraged to enter clinical trials to increase the number and improve the quality of IGRT protocols in their centre.

**SITE SPECIFIC PROTOCOLS**

This section details site specific recommendations for imaging. However there are principles which apply to all sites and should be considered. For example:

- Effective immobilisation should be used to reduce the set-up errors.
- Indexing (putting the immobilisation system and therefore the patient in the same place on the treatment couch for each fraction) minimises systematic errors from variable couch sag.
- It is important for all centres to audit the accuracy of their immobilisation equipment (as recommended in 'On Target') to calculate the systematic and random uncertainties in order to establish departmental PTV margins and therefore the on-treatment verification frequency required. This will be useful when deciding the appropriate action level, which should be used for the IGRT technique.
- For volumetric imaging it is crucial that a volume(s) or region of interest is defined without ambiguity in order to allow for reliable automated matching.

It must also 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.

The common sites included are listed below (the guidelines have not covered rarer tumours such as soft tissue sarcomas or paediatrics).

- **Breast**
- **Central Nervous System**
- **Gastro-intestinal System**
- **Gynaecology**
- **Head and Neck**
- **Lung**
- **Urological**

## Breast

**Background:** IGRT for breast radiotherapy based on megavoltage portal imaging has been used generally to assess reproducibility. This is well documented in the 'On Target' report. There is little evidence currently showing the impact of IGRT on the reduction in the volume of normal breast irradiated with high dose, or reduced organ at risk exposure. For left sided breast tumours it is important to consider the dose to the heart in particular. Clinical trials, such as the UK IMPORT High trial (Coles et al 2006), which use complex treatment plans to deliver escalated dose to the tumour bed have a requirement for more sophisticated imaging and correction protocols to achieve tight PTV margins (Coles et al 2011). Studies associated with the trial are investigating the consequences of using IGRT, and the results of this work are likely to inform recommendations in the next five years.

**Immobilisation and Reproducibility:** Effective immobilisation can be achieved using a breast board (commercial, or custom) with adjustable arm supports, head rest, bottom stop and knee support, is necessary for good quality breast radiotherapy treatment. Both arms should be raised where possible to achieve a more stable position.

Where appropriate immobilisation is used, population systematic errors and population random errors are of the order of 3 – 4 mm each as detailed in the 'On Target' report.

Breath-hold techniques (e.g. deep inspiration breath hold) and respiratory-gating can be used to reduce the dose to the heart and could be considered where an unacceptable large volume of heart would be irradiated otherwise.

The British Association of Surgical Oncology recommend best practice is to insert clips after breast conservation surgery. These can be used to aid localisation and verification.

It is important that magnitude of population set-up errors is quantified in the individual department particularly prior to any introduction of complex planning, such as simultaneous integrated boost.

**Pre-Treatment Imaging:** CT scanning with a maximum slice thickness of 5mm is recommended to provide accurate dosimetry throughout the breast and quantify dose to OAR.

It is common for anatomical borders to be used to determine whole breast and chest wall radiotherapy fields. These provide consistency, particularly for clinical trials because clinician definition of CTV has been shown to be very variable (Coles et al 2011). The field borders may be used to create a volume for plan evaluation. As the ICRU 50/62 model is not used explicitly this volume is not related directly to a PTV but fulfils some of that function.

If a breast CTV is delineated, a PTV margin of 10-15 mm would be required for typical population set up errors. It is possible the fields may be unacceptably large compared to those derived from anatomical landmarks.

**On-treatment verification:** Light fields, and parameters such as a midline FSD, are used to assess patient set up, however these on their own are insufficient to assess organ at risk overexposure, and radiation-based verification is required. Lung depth measurement can be used to assess reproducibility and to confirm that lung tissue is not overexposed.

A suitable tolerance for a gross error check of set up is 5mm. If exceeded, it is advised that the patient's set-up is checked and re-imaged. If the tolerance is still exceeded re- simulation/replanning is advised.

Conformal photon treatments to the partial breast; sequential tumour bed boost conformal photon plans and simultaneous integrated boost treatments all require 2D paired images or 3D imaging, and the use of fiducial markers, to determine set-up errors accurately. This is particularly important if the tumour bed PTV margin is small e.g. 5mm.

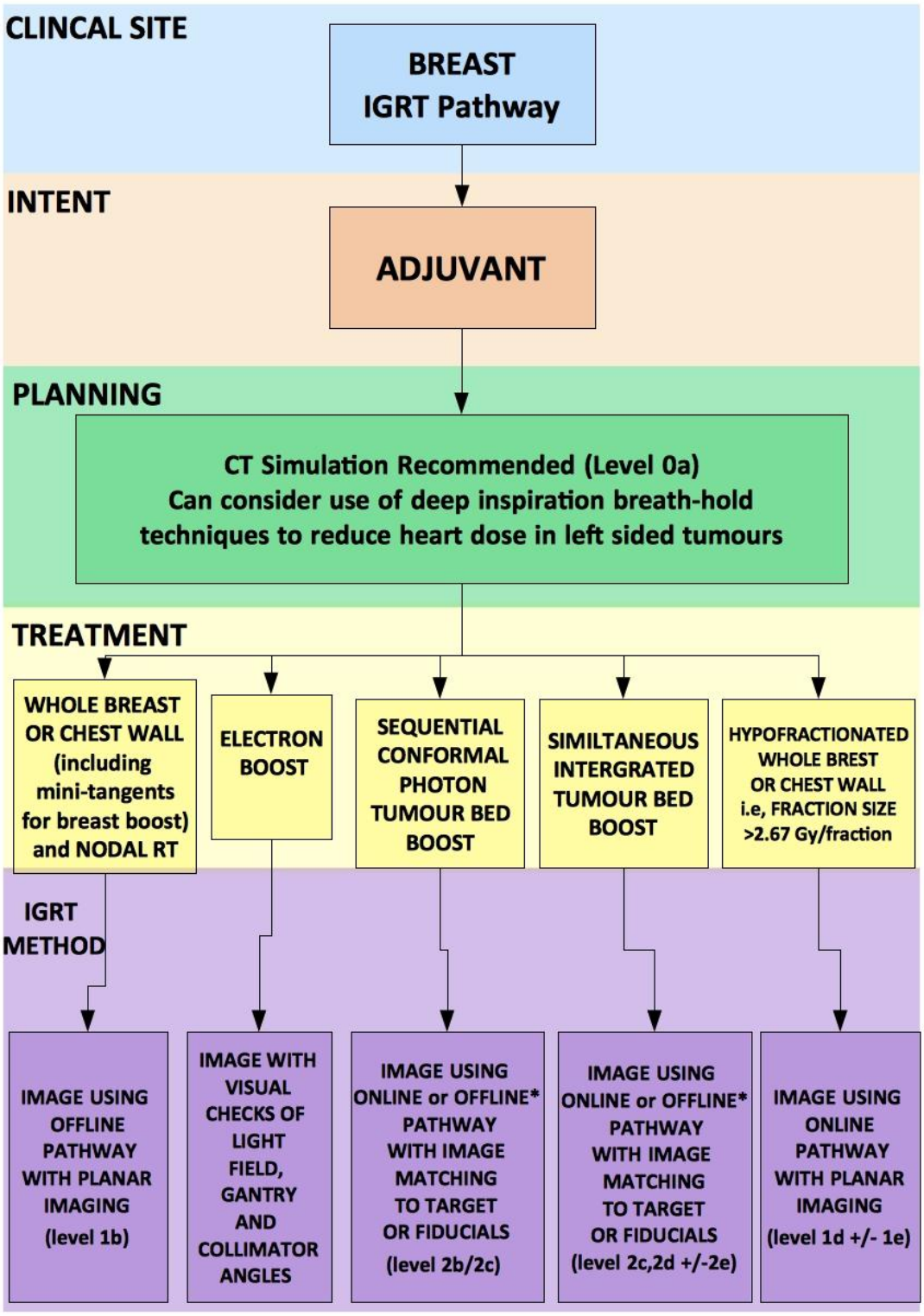
**Site Specific Issues:** Tangential fields alone do not enable the exact resolution of errors into the three cardinal directions (sup-inf, ant-post, left-right). They may be used, however, to derive any systematic errors in the plane of the image. This information may be used, along with midline FSD and light field border information, to indicate the source of the error e.g. the patient has slipped down the breast board, or the lung depth is too large, implying the medial field may be falling too close to the midline, or the lateral field too posterior. Small adjustments (≤3 mm) may be made to the patient position, mid line pin and/or field borders to compensate.

2D imaging (with a non opposed pair of images) and 3D volumetric imaging resolve the displacements in sup-inf, ant-post and left-right directions accurately. Both have the potential to increase the time and dose burden, which may not be appropriate for whole breast, or chest wall treatments, with standard borders, or where 10-15 mm PTV margins are used.

For large breast patients, customised shell or prone position may be required to optimise dosimetry.

**References:**


1. 1. On Target: Ensuring Geometric Accuracy In Radiotherapy. A joint report published by the Society and College of Radiographers, the Institute of Physics and Engineering in Medicine and The Royal College of Radiologists. http://www.rcr.ac.uk/publications.aspx?PageID=149&PublicationID=292
2. Coles CE, Harris EJ, Donovan EM, Bliss P, Evans PM, Fairfoul J, Mackenzie C, Rawlings C, Syndikus I, Twyman N, Vasconcelos J, Vowler SL, Wilkinson JS, Wilks R, Wishart GC, Yarnold J. Evaluation of implanted gold seeds for breast radiotherapy planning and on treatment verification: a feasibility study on behalf of the IMPORT trialists. Radiother Oncol. 2011 Aug;100(2):276-81.
3. Coles CE, Wishart G, Donovan E, Harris EJ, et al. Evaluation of implanted gold seeds for breast radiotherapy planning and on treatment verification. Radiother Oncol 2011;100:276-281.




* Especially if significant changes seen in 1st 3-5 fractions

**Central Nervous System (CNS) tumours**

**Background:** Unlike many tumour sites, in the structures in the brain are not subject to large changes in internal position, being constrained by bony structures. Image guidance therefore centres on imaging bony structures to ensure that patient positioning is correct.

**Immobilisation and positioning:** For radical radiotherapy of cranial tumours, the location will determine whether the patient should be positioned prone or supine. Supine has the advantage of comfort for the patient and ease of positioning on the treatment couch. For posterior brain lesions, it may be necessary to treat prone because of the greater scope in field directions. However if couch extensions are available where the patient can be positioned more superiorly, off the couch end, a supine position may be possible.

For fractionated supine treatments two types of immobilisation are available: a beam direction shell (BDS) and a relocatable stereotactic head frame. The positioning reproducibility of the shell is influenced by the number of fixation points of the shell to the base board [1]. Personalised headrests can be used. If using a perspex BDS the treatment portals should be cut out without compromising rigidity, to improve skin sparing.

The set up error using immobilisation masks ranges from approximately 3mm using high melting point acrylic systems [2,3] to 5mm using low melting point thermoplastic systems [3]. It is important the magnitude of patient population set up errors is quantified in individual departments, depending on the immobilisation used.

A relocatable stereotactic frame can deliver a higher precision in repositioning, reducing both systematic and random errors, and therefore reducing the CTV to PTV margin accordingly. The overall error of a relocatable stereotactic frame is in the region of 2 - 2.5mm [4]. For radiosurgery treatments a fixed head frame is commonly used, to minimise set up errors.

Craniospinal treatments have traditionally been undertaken using prone positioning with the patient in a mask. This enables palpation of the spine to assist with patient set-up and visualisation of field junctions. However the use of a supine technique is increasing. This may have advantages for patients requiring general anaesthesia, where the maximum FSD is not adequate to treat the spine, or for patient comfort. Planning solutions to treat the patients supine have recently been described [5]. However, more rigorous patient immobilisation is required, including a mask extending down to the shoulders and reproducible positioning of the pelvis and legs [5].

**Pre-treatment imaging:** CT scanning should be used using scan slice thickness of ≤3mm. IV contrast may be helpful, and co-registered MRI should normally be used for target localisation. This may be a pre- or post-operative imaging set, or indeed both.

**On-treatment imaging:** For the majority of brain and spinal tumours, verification of target position can be done by comparing bony anatomy positions, as the tumours are fixed within the confines of the skull or vertebrae. The on-treatment imaging frequency will vary according to the radiotherapy method and PTV margin used.

For fractionated treatment of brain and spinal tumours, calculation and correction of systematic error requires, as a minimum, off-line imaging for the first 3 fractions followed by a position

correction for the rest of the course. Weekly imaging is useful to monitor for trends over the treatment course, such as changing fit of the immobilisation device from weight gain (e.g. from steroids) or hair loss.

For IMRT and fractionated stereotactic radiotherapy, the same systematic error reduction protocols should be used as the minimum standard. However, where available, online random set-up error detection and reduction systems should be used, imaging immediately before each fraction and correcting before delivery.

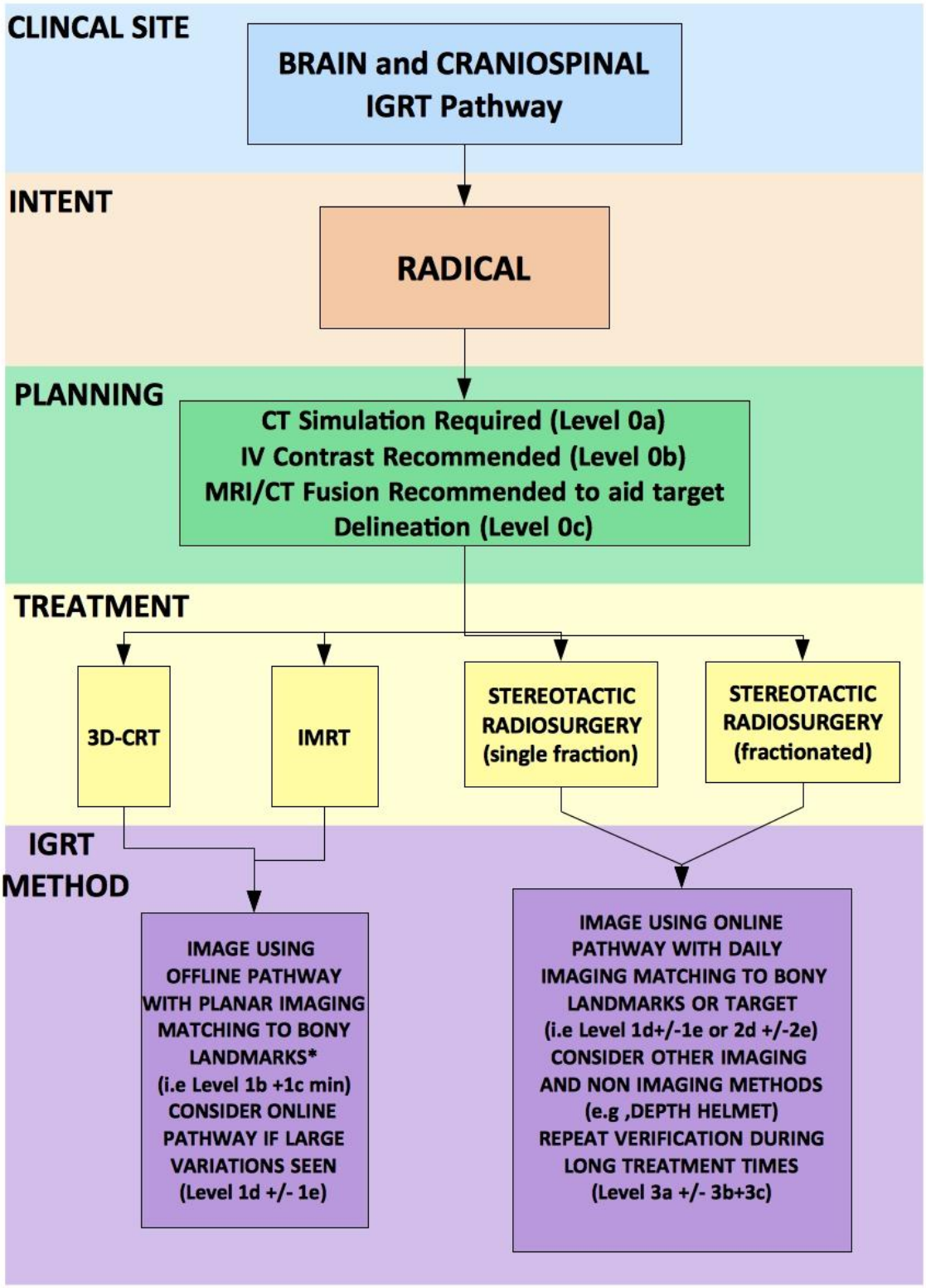
For stereotactic radiosurgery performed using a relocatable frame, or for frameless radiosurgery, online imaging should be utilised. In addition, the relocation of the frame to the patient can be verified using non-imaging systems such as a depth helmet [4] or optical surface imaging.

For craniospinal IMRT solutions, more detailed on-treatment imaging is needed to ensure reproducibility. The position of the cranial fields is the priority and it is essential to verify the junction. Different margins can be planned for different spinal levels to account for any increased uncertainty. These principles particularly apply to supine positioned treatments.

**Site specific Issues**: In the case of craniopharyngioma, fluid accumulation within cystic remnants may rarely cause enlargement during treatment; this is usually associated with visual symptoms which would require urgent MR imaging and neurosurgery. Some authors have advocated weekly diagnostic imaging to verify that the target has not changed [6].

**References:**


1. Gilbeau L, Octave-Prignot M, Loncol T, Renard L, Scalliet P, Gregoire V. Comparison of setup accuracy of three different thermoplastic masks for the treatment of brain and head and neck tumors. *Radiother Oncol* 2001; 58: 155-162.
2. Hanna CL, Slade S, Mason MD, Burnet NG. Translating radiotherapy Clinical Target Volumes into Planning Target Volumes for bladder and brain tumour patients. *Clin Oncol* 1999; 11: 93-98
3. Boda-Heggemann J, Walter C, Rahn A, Wertz H, Loeb I, Lohr F, Wenz F. Repositioning accuracy of two different mask systems-3D revisited: comparison using true 3D/3D matching with cone-beam CT. *Int J Radiat Oncol Biol Phys*. 2006; 66(5): 1568-75.
4. Burton KE, Thomas SJ, Whitney D, Routsis DS, Benson RJ, Burnet NG. Accuracy of a relocatable stereotactic radiotherapy head frame evaluated by use of a depth helmet. *Clin Oncol (R Coll Radiol)*. 2002; 14(1): 31-9.
5. Parker W, Filion E, Roberge D, Freeman CR. Intensity-modulated radiotherapy for craniospinal irradiation: target volume considerations, dose constraints, and competing risks. *Int J Radiat Oncol Biol Phys*. 2007; 69(1): 251-7.
6. Beltran C, Naik M, Merchant TE. Dosimetric effect of target expansion and setup uncertainty during radiation therapy in pediatric craniopharyngioma. *Radiother Oncol*. 2010; 97: 399-403.




*Volumetric imaging and soft tissue matching may be required in rare circumstance when changes in the soft tissue anatomy are more likely e.g. craniopharyngiomas where fluid can accumulate during treatment.

## Gastro-Intestinal System

### Upper gastro-intestinal (including Upper GI and hepatobilliary)

**Background:** Upper GI malignancies include oesophageal, stomach, pancreas and hepatobilliary cancer. All sites can be challenging to define the GTV and loco-regional lymph nodes and are affected by respiratory and peristaltic organ motion.

**Immobilisation and Reproducibility:** The level of IGRT depends on the treatment intent, complexity and the set-up margins. Immobilisation can be used to reduce the set-up error component of the margin. All patients should have CT scanning for planning. For upper 1/3 oesophagus tumours the patients should be immobilised supine, arms down with 5 point thermoplastic mask, (as in head and neck tumours).

For mid, lower, GOJ (gastro-oesophageal junction) and pancreas tumours use lung board with arms up and knee pads.

**Pre-Treatment Imaging:** For planning the CT slice thickness should not be larger than 3mm, with IV contrast standard for all radical patients. In case of induction chemotherapy and more than 10% weight loss, a second planning CT is often necessary. For tumour and at risk nodal areas definition pre-treatment imaging such as Endoscopic ultrasound (EUS), PET or MRI should be used.

The margins used will depend on the individual centre. The recommended margins to compensate for patient set-up are between 5mm and 7mm which is derived from a summary of published studies of patients receiving radical radiotherapy to the oesophagus (>15 fractions)[1,2]. All images were taken pre-treatment. Studies of set-up motion of radical lung patients with centrally located tumours may also be relevant when same immobilisation is used[3].

For pancreatic cancer larger margins are necessary particularly in the superior inferior direction and will depend on whether mid-respiratory position of the tumour is known[4].

For mobile tumours (gastro-oesophageal junction [GOJ] and pancreas) 4DCT is recommended to derive patient specific margins and identify those patients where motion control/gating may be appropriate. If 4DCT is not available a set-up margin should be used based on the individual centre and is typically 5-7 mm circumferential and up to 10 mm cranial caudal direction. Asymmetric margins should be considered depending on the tumour location[5,6].

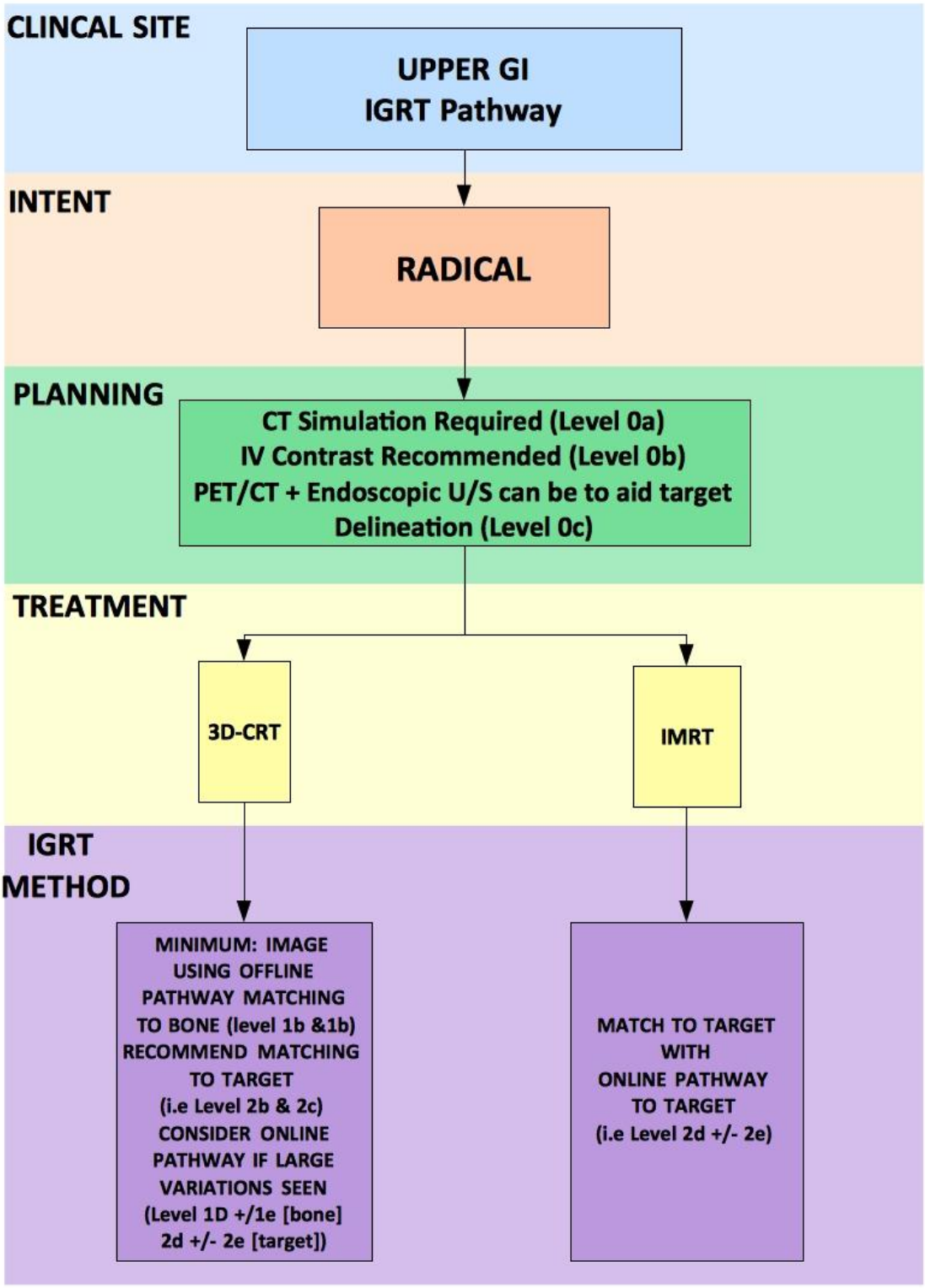
**On Treatment Imaging:** For upper 1/3 tumours treated with IMRT/3DCRT see head and neck chapter for verification. Volumetric imaging is recommended as standard – if available. The volume of match includes the PTV and a 1 cm 3D margin. Automated bone match should be considered in the first instance with an off-line protocol.

**Site Specific Issues:** Patients can have significant weight loss on treatment with a consequent change in separation and therefore dosimetry. If significant weight loss occurs consider formal dosimetric analysis and re-planning. If an oesophageal stent in present this needs to be monitored for stent migration. Rotation can also be a significant issue and can be quantified using volumetric imaging. We suggest that if the rotation is >5° then consider repositioning and re-imaging the patient before treatment.

Stents should be used with caution as surrogates for tumour position as there is a risk of migration.

**References:**


1. Chen YJ, Han C, Liu A, et al. Setup variations in radiotherapy of esophageal cancer: evaluation by daily megavoltage computed tomographic localization. Int J Radiat Oncol Biol Phys 2007;68:1537-1545.
2. Hawkins MA, Aitken A, Hansen VN, McNair HA, Tait DM. Set-up errors in radiotherapy for oesophageal cancers--is electronic portal imaging or conebeam more accurate? Radiother Oncol. 2011 Feb;98(2):249-54
3. Yeung AR, Li JG, Shi W, Newlin HE, Chvetsov A, Liu C, Palta JR, Olivier K. Tumor localization using cone-beam CT reduces setup margins in conventionally fractionated radiotherapy for lung tumors. Int J Radiat Oncol Biol Phys. 2009 Jul 15;74(4):1100-7
4. Whitfield G, Jain P, Green M, Watkins G, Henry A, Stratford J, Amer A, Marchant T, Moore C, Price P. Quantifying motion for pancreatic radiotherapy margin calculation. Radiother Oncol. 2012 Mar 10.
5. Matzinger O, Gerber E, Bernstein Z, Maingon P, Haustermans K, Bosset JF, Gulyban A, Poortmans P, Collette L, Kuten A. EORTC-ROG expert opinion: radiotherapy volume and treatment guidelines for neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction and the stomach. Radiother Oncol. 2009 Aug;92(2):164-75.
6. Goldstein SD, Ford EC, Duhon M, McNutt T, Wong J, Herman JM. Use of respiratory-correlated four-dimensional computed tomography to determine acceptable treatment margins for locally advanced pancreatic adenocarcinoma. Int J Radiat Oncol Biol Phys. 2010 Feb 1;76(2):597-602


CLINCAL SITE
UPPER GI
IGRT Pathway
INTENT
RADICAL
PLANNING
CT Simulation Required (Level 0a)
IV Contrast Recommended (Level 0b)
PET/CT + Endoscopic U/S can be to aid target
Delineation (Level 0c)
TREATMENT
3D-CRT
IMRT
IGRT
METHOD
MINIMUM: IMAGE
USING OFFLINE
PATHWAY MATCHING
TO BONE (level 1b &1b)
RECOMMEND MATCHING
TO TARGET
(i.e Level 2b & 2c)
CONSIDER ONLINE
PATHWAY IF LARGE
VARIATIONS SEEN
(Level 1D +/1e [bone]
2d +/- 2e [target])
MATCH TO TARGET
WITH
ONLINE PATHWAY
TO TARGET
(i.e Level 2d +/- 2e)

**Lower Gastro-Intestinal (Rectal)**

**Background:** A number of studies have shown a correlation between radiotherapy dose to small bowel and long-term toxicity. Consequently there has been a move away from orthogonal fields towards conformal and IMRT techniques where there is a reduction in the dose to organs at risk with adequate coverage of the target volume. For this reason there is a need for a greater understanding of the movement of the GTV and the components of the CTV including the rectum, mesorectum and pelvic nodes. The movement of the rectum in rectal cancer has been less well studied compared with the movement in prostate and bladder cancer. Furthermore it cannot be assumed that the rectum in the presence of a cancer will move in the same way as the normal rectum. However a number of small studies have attempted to define the movement of in particular the mesorectum and provide the main evidence for IGRT at this site.

Movement of the rectum/mesorectum has been studied in a number of ways including repeated CT planning scans, repeated MRI, megavoltage CT and cone beam CT. Whilst the rectum is relatively easy to see on CBCT the mesorectum is less well visualised. To over come this the Dutch group have defined a volume, called the MesoRect, as the rectum and mesorectal fat starting at the dentate line up to the last CT-slice where the lateral borders of the mesorectal fascia were still visible[1]. However this is not widely clinically used

The CTV for rectal cancer also includes at risk nodal groups in particular the internal iliacs. Nodal groups follow the vessels and are thought to be relatively fixed compared with the mesorectum.

**Immobilisation:** Patients should be treated prone with a comfortably full bladder. The justification for this position relates to displacing small bowel out of the pelvis and reducing toxicity. However, the prone position is associated with more set-up errors and is often too uncomfortable for patients with a stoma.

Bellyboards are used by some centres. The advantage is a reduction in small bowel and this has been confirmed in a number of studies[2]. The disadvantage is the discomfort especially for male patients and those with a stoma.

Studies in all tumour sites, including rectal have shown a large intra-patient variation of the bladder volume over a prolonged treatment course. Rectal preparations such as enemas or laxatives are probably inappropriate for patients who are often symptomatic from their rectal cancer.

**Pre-treatment Imaging:** CT planning is recommend with Oral and IV contrast[3].

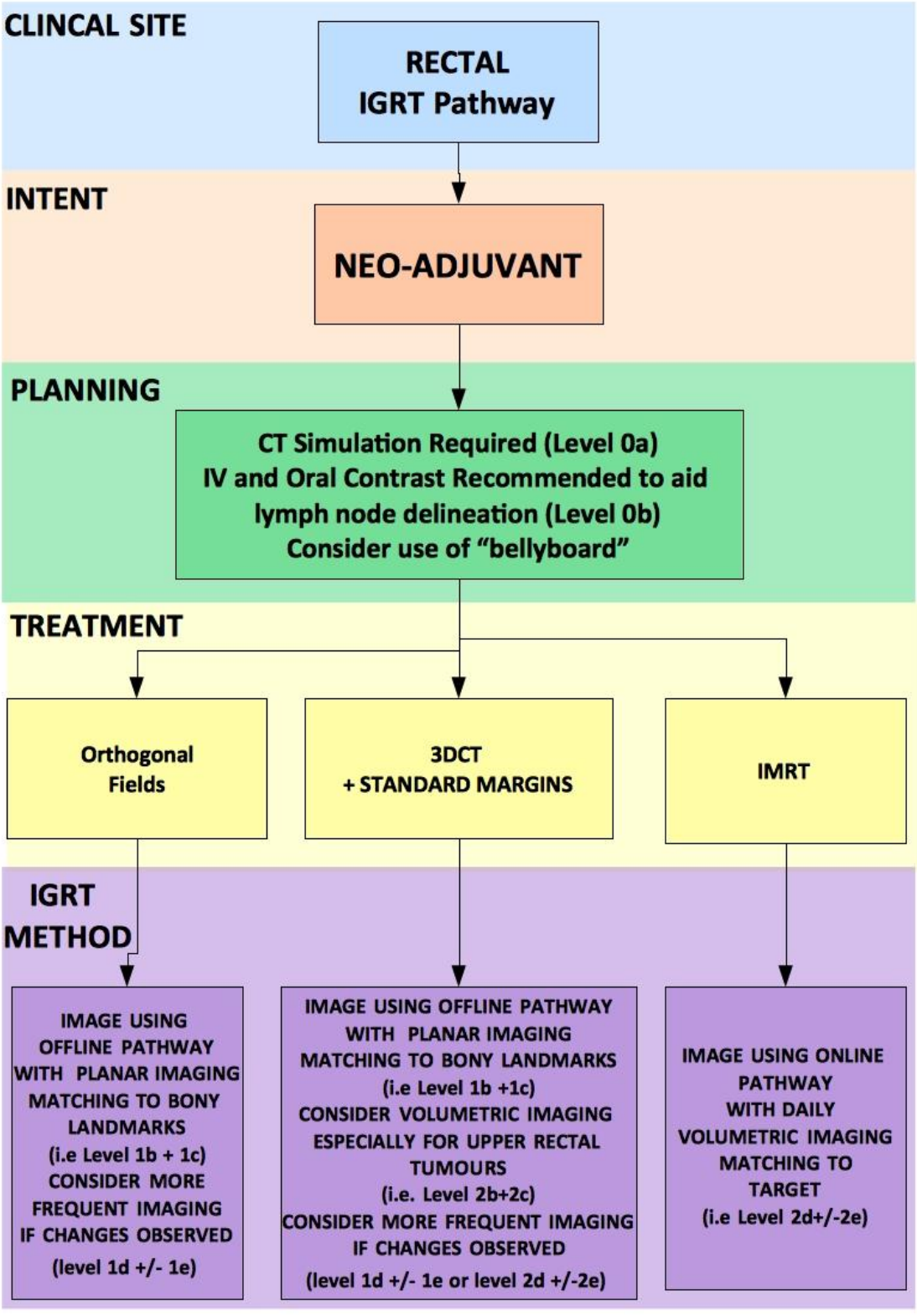
Pre-treatment MRI should be used to aid tumour delineation.

**On treatment Imaging:** For orthogonal fields planar imaging matching to bone is acceptable. For upper rectal and more complex RT delivery techniques volumetric imaging is recommended.

For pre operative short fractionated treatment daily imaging should be considered.

**References:**


1. Nijkamp J, de Jong R, Sonke JJ, Remeijer P, van Vliet C, Marijnen C. Target volume shape variation during hypo-fractionated preoperative irradiation of rectal cancer patients. Radiother Oncol. 2009 Aug;92(2):202-9.
2. Gwynne S, Mukherjee S, Webster R, Spezi E, Staffurth J, Coles B, Adams R. Imaging for target volume delineation in rectal cancer radiotherapy--a systematic review. Clin Oncol (R Coll Radiol). 2012 Feb;24(1):52-63.
3. Wiesendanger-Wittmer EM, Sijtsema NM, Muijs CT, Beukema JC. Systematic review of the role of a belly board device in radiotherapy delivery in patients with pelvic malignancies. Radiother Oncol. 2012 Mar;102(3):325-34.


CLINCAL SITE
RECTAL
IGRT Pathway
INTENT
NEO-ADJUVANT
PLANNING
CT Simulation Required (Level 0a)
IV and Oral Contrast Recommended to aid
lymph node delineation (Level 0b)
Consider use of "bellyboard"
TREATMENT
Orthogonal
Fields
3DCT
+ STANDARD MARGINS
IMRT
IGRT
METHOD
IMAGE USING
OFFLINE PATHWAY
WITH PLANAR IMAGING
MATCHING TO BONY
LANDMARKS
(i.e Level 1b + 1c)
CONSIDER MORE
FREQUENT IMAGING
IF CHANGES OBSERVED
(level 1d +/- 1e)
IMAGE USING OFFLINE PATHWAY
WITH PLANAR IMAGING
MATCHING TO BONY LANDMARKS
(i.e Level 1b +1c)
CONSIDER VOLUMETRIC IMAGING
ESPECIALLY FOR UPPER RECTAL
TUMOURS
(i.e. Level 2b+2c)
CONSIDER MORE FREQUENT IMAGING
IF CHANGES OBSERVED
(level 1d +/- 1e or level 2d +/-2e)
IMAGE USING ONLINE
PATHWAY
WITH DAILY
VOLUMETRIC IMAGING
MATCHING TO
TARGET
(i.e Level 2d+/-2e)

**Gynaecological**

**Background:** There are two situations to consider with respect to IGRT and the treatment of gynaecological cancer; where the uterus is intact and the post-operative pelvis.

**Treatment of the intact uterus*:*** When treating carcinoma of the cervix radically, it is usually accepted that the whole of the uterus needs to be included in the volume. Uterine movement can vary significantly (up to 3cm in the anterior-posterior direction) this motion is independent of bony anatomy. Bladder filling has been shown in several studies to influence uterine movement although correlation is weak. Movement in both the anterio-posterior (AP) and superior-inferior (SI) directions have been reported. Movement of the cervix including the GTV for cervical cancer and upper vagina in the AP direction have been correlated with rectal filling. In addition there are studies that have looked at the impact of tumour regression of cervical cancer during treatment. Where significant regression occurs during treatment the possibility of re-planning has been discussed allowing a reduction in the volume of normal tissue exposed.

**Post-operative pelvis*:*** There have been fewer studies in the post-operative pelvis. In this situation the CTV is composed of the upper vagina and nodal groups. Nodal groups follow vessels which are fixed relative to bony anatomy. However, the vaginal vault moves with changes in rectal filling in the AP direction The impact of bladder filling is less clear but again the main influence is in the AP direction. There is very little movement of the vagina in the left-right direction[1,2].

**Immobilisation and Reproducibility:** Whilst the prone position has been shown to reduce small bowel volume in the pelvis the supine position is more reproducible. Attention should be made to bladder filling. Whilst an empty bladder volume might be easier to reproduce, this will lead to increased dose to small bowel and bladder. In the post-operative pelvis two planning scans have been advocated, one with an empty bladder and one with a full bladder. Images are fused and planning can then take account of the position of the vagina in these two extremes.

Whilst rectal preparation has not been widely used in gynaecological cancer due to the risk of diarrhoea associated with treatment it is now recognised that rectal filling can influence the position of the vaginal vault in the post-operative pelvis and to a lesser extent the cervix. Rectal filling at the time of the planning scan should be assessed and intervention/re-planning considered if volumes are large and pushing the vaginal vault anteriorly.

**Pre-treatment imaging:** CT scanning using slice thickness of 3mm or less with IV contrast to aid delineation of lymph nodes should be used. Oral contrast may also be used to aid delineation of the bowel. Pre-treatment MRI and PET/CT can be used to aid target delineation.

**On-treatment imaging:** Despite the lack of evidence to inform the use of IGRT in gynaecological external beam RT, given the uncertainty of internal organ motion, more generous margins around the uterine and vaginal CTV are required if bone matching alone is being used. If good quality soft tissue imaging is available then smaller margins around CTV are possible. Hence, for 3D-CRT with conventional margins in patients with an intact uterus we recommend volumetric imaging matching to the soft tissue including the bladder and uterus. As a minimum the offline protocol should be used for the first 3-5 fractions and then repeat weekly. In post-operative setting for standard 3D-CRT

with conventional margins the minimum standard is matching to bony landmarks with planar imaging using the offline matching protocol and repeating this at least weekly[3,4,5].

**Site Specific issues:** Whilst there are a number of studies that have examined movement of soft tissue in the AP/SI/RL position rotation (also called 'pelvic tilt') has rarely been discussed. Where this is seen then care should be taken in moving treatment fields. Manipulations to correct rotation can result in the PTV moving out of the field and where significant re-planning should be considered.

IMRT techniques should only be used both for the intact and post-operative pelvis if soft tissue imaging is available and using the online imaging protocol to reduce random error. Any change in CTV margin should ideally be performed in the context of a clinical trial or prospective audit.

**References:**

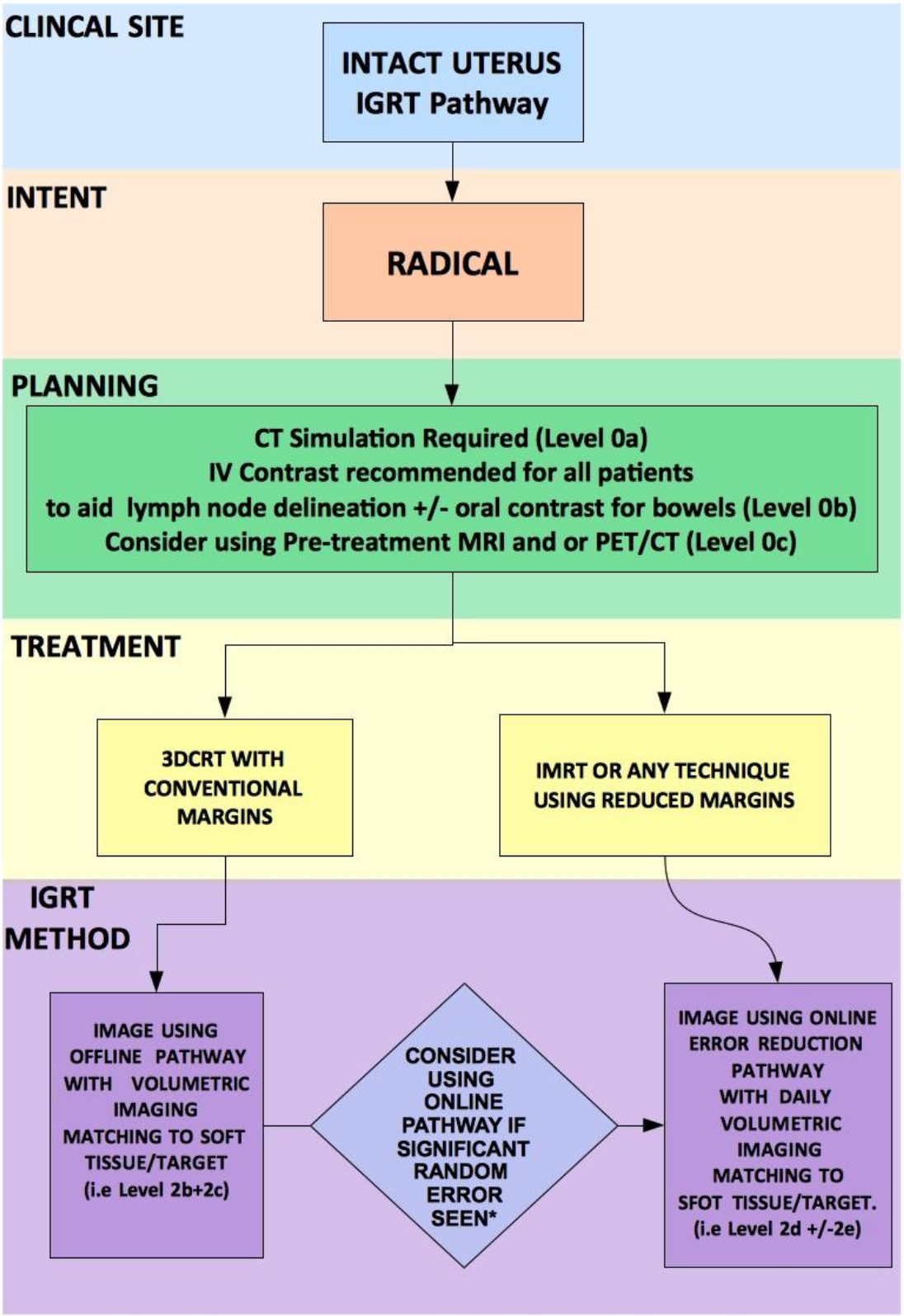

1. Jhingran A, Salehpour M, Sam M, Levy L, Eifel PJ. Vaginal motion and bladder and rectal volumes during pelvic intensity-modulated radiation therapy after hysterectomy. Int J Radiat Oncol Biol Phys. 2012 Jan 1;82(1):256-62.

2. Jürgenliemk-Schulz IM, Toet-Bosma MZ, de Kort GA, Schreuder HW, Roesink JM, Tersteeg RJ, van der Heide UA. Internal motion of the vagina after hysterectomy for gynaecological cancer. Radiother Oncol. 2011 Feb;98(2):244-8.

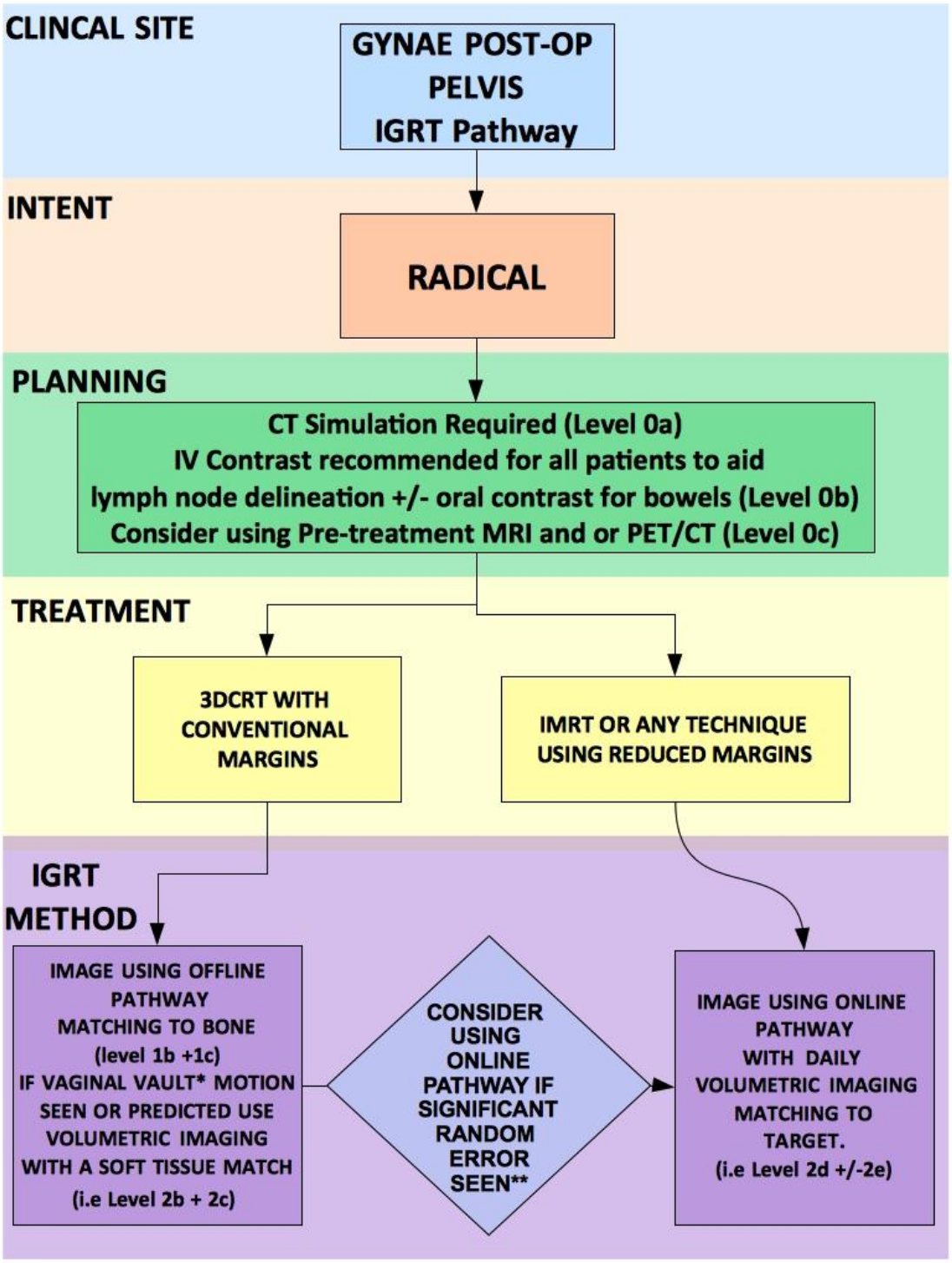
3. Haripotepornkul NH, Nath SK, Scanderbeg D, Saenz C, Yashar CM. Evaluation of intra- and inter-fraction movement of the cervix during intensity modulated radiation therapy. Radiother Oncol. 2011 Mar;98(3):347-51.

4. Taylor A, Powell ME. An assessment of interfractional uterine and cervical motion: implications for radiotherapy target volume definition in gynaecological cancer. Radiother Oncol. 2008 Aug;88(2):250-7.

5. Beadle BM, Jhingran A, Salehpour M, Sam M, Iyer RB, Eifel PJ. Cervix regression and motion during the course of external beam chemoradiation for cervical cancer Int J Radiat Oncol Biol Phys. 2009 Jan 1;73(1):235-41.




*Typically this due to large variations in the uterine position




*Some centres are using implanted markers to visualise the vaginal vault on planar imaging

**Typically this due to large variations in the vaginal vault position

**Head & Neck**

**Background:** Radiotherapy as definitive or post-operative therapy often in conjunction with chemotherapy is widely utilized in the management of patients with head and neck cancer. Standard fractionations will involve three, four, six and seven week daily schedules. Level 1 evidence is in support of IMRT for large volume sites that require irradiation.

Treatment invariably impacts on the nutritional status of patients and despite aggressive measures to support this side effect can result in clinically significant weight loss affecting the tolerance of treatment, set up accuracy and the speed of recovery from such intensive schedules.

**Immobilisation and patient positioning:** Patients will be immobilised in the supine position and a 5 point fixation system, fixated at the head, neck and shoulders is recommended. The actual position of the head i.e. flexed, neutral or extended will be determined by the primary site of irradiation and thus orientation of treatment beams. This should be specified at the time of manufacturing the immobilisation device.

**Pre-treatment Imaging:** All patients should have CT planning to define accurately the target volume, normal tissues and precise planning. Planning CTs should be of 2.5-3.0mm maximum slice thickness with IV contrast to aid in target volume delineation. Co-registration of diagnostic and ideally dedicated MRI and PET images are optimal in defining precisely the target volumes and in determining key normal tissues (e.g. chiasm). OARs that require visualization and outlining include spinal cord, brainstem, brain, parotid glands. OARs that require visualization and outlining for optimal planning include other major salivary glands, larynx, oesophagus, oral cavity, cochlea. Typical CTV-PTV margins will be of the order of 3-4mm in all directions but will need to be determined locally.

**On-treatment Imaging:** A minimum standard should be daily on line (2D) planar imaging as this will give confidence using pre-determined bony landmarks that delivery of precisely defined radiotherapy is as intended. A specific area of interest can be defined to aid verification of position with reference to the organs at risk e.g. spinal cord.

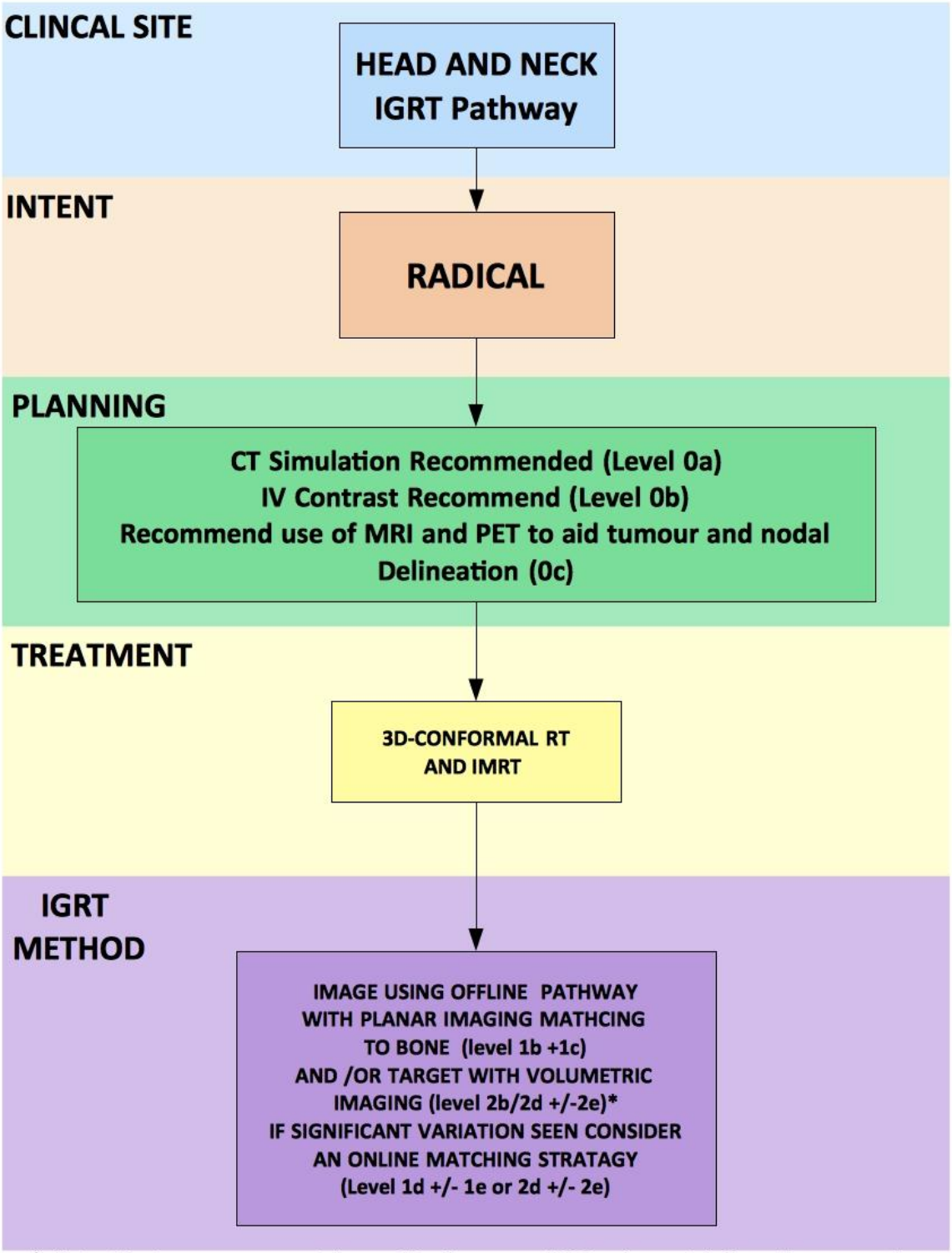
Volumetric (3D) imaging has demonstrated potentially significant changes in normal tissue doses during a course of radiotherapy with non-adaptive IGRT strategies. 3D (volumetric) imaging may not give equivalence to 2D (planar) imaging in determining alignments and will need to considered if both approaches are to be used in conjunction.

**Site Specific Issues:** Given that weight loss (despite active measures to address this), tumour shrinkage and tissue oedema can all influence the patient's anatomy, a volumetric approach could be considered ideal. This will facilitate **delivered** dose distributions to the tumour volumes and normal tissues and may lead to revisions of treatment plans as appropriate.

The precise strategy for adaptive re-planning will need to be determined both as a generalization nationally but also at a local level according to equipment characteristics.

**References:**


1. Li H, Zhu XR, Zhang L, Dong L, Tung S, Ahamad A, Chao KS, Morrison WH,Rosenthal DI, Schwartz DL, Mohan R, Garden AS. Comparison of 2D radiographic images and 3D cone beam computed tomography for positioning head-and-neck radiotherapy patients. Int J Radiat Oncol Biol Phys. 2008 Jul 1;71(3):916-25.
2. Graff P, Hu W, Yom SS, Pouliot J. Does IGRT ensure target dose coverage of head and neck IMRT patients? Radiother Oncol. 2011 Dec 5. [Epub ahead of print]
3. van Kranen S, van Beek S, Mencarelli A, Rasch C, van Herk M, Sonke JJ. Correction strategies to manage deformations in head-and-neck radiotherapy. Radiother Oncol. 2010 Feb;94(2):199-205.
4. Castadot P, Geets X, Lee JA, Grégoire V. Adaptive functional image-guided IMRT in pharyngo-laryngeal squamous cell carcinoma: is the gain in dose distribution worth the effort? Radiother Oncol. 2011 Dec;101(3):343-50.




* Note that measurement from 2D planar and 3D volumetric imaging may give different results on same image and needs to be considered if a combination of 2D and 3D imaging are to be used. The advantage of 3D volumetric imaging allows for tumour and nodes to be visualised during RT course

## LUNG CANCER

**Background:** Many factors make lung tumours one of the most complex radiotherapy sites to plan and treat accurately. At the planning stage numerous studies have shown inter-observer variation in GTV delineation[1] that can be reduced by the use of PET-CT in the planning process[2] particularly in help to define the GTV in areas of lung collapse.

At treatment delivery IGRT is complex because; (1) lung tumours are difficult to see with megavoltage portal imaging, (2) lung tumours can move significantly with respiration and mediastinal organ movement in all three directions and (3) during treatment significant changes in the external anatomy (e.g. weight loss) and internal anatomy (e.g. tumour increase/decrease, collapse or re-inflation of the lung) can occur.

Lung motion occurs independent of bone anatomy and therefore for the vast majority of lung tumours to deliver the radiotherapy accurately, the lung cancer must be imaged directly using volumetric imaging or a surrogate such as implanted fiducial markers or transponders[3].

For patients with significant tumour movement (typically >0.5cm) motion management strategies can be used. The choice of strategy will depend on the individual centre's equipment but can include breath hold techniques, gating based on external and internal surrogates, accounting for motion in margins, or abdominal compression. These systems need to checked and monitored closely to ensure that they are appropriate for each individual patient. The method of IGRT required depends on the treatment intent, the size of the PTV margins planned/needed and the fractionation schedule. As a significant amount of lung cancer radiotherapy is palliative we have divided the IGRT strategy into palliative and radical.

**Immobilisation and Reproducibility:**

Immobilisation should be used to reduce the set-up error component of the calculated PTV margin and should be appropriate for the intended use (both radical and palliative lung treatments).

Radical treatments need immobilisation systems that constrain patient movement to help reproduce the patient's position throughout the treatment course. This can be achieved using rigid immobilisation systems such as 'wing, thoracic or breast boards'. These can hold the patient's arms above the head to allow unrestricted access to the thorax, where needed; some are inclined to aid patient breathing.

Palliative treatments can require greater levels of patient comfort, as patients are more likely to be emaciated and suffer from greater discomfort. Higher levels of elevations should be available to aid breathing; materials should be softer to help with pain. This should aid some patients so that they are able to maintain the same position for longer.

For most thoracic tumour locations, elevating both arms aids stability and reproducibility. Indexing (putting the immobilisation system and therefore the patient in the same place on the treatment couch for each fraction) minimises systematic errors from couch sag. Exceptions are for apical

tumours (e.g. Pancoast tumours) where planning with the arms down with a moulded shell may be more appropriate.

Indexed knee supports improve patient comfort and treatment reproducibility by increasing the surface area contact of the patient to the couch.

SABR treatments will require high levels of treatment accuracy and immobilisation may therefore need to be improved either by adapting the current system (e.g. adding customised vac bag, chin strap,) or using specific SABR immobilisation devices.

It is important for all centres to audit the accuracy of their immobilisation equipment (as recommended in 'On Target') to calculate the systematic and random uncertainties for all anatomical sites. This will be useful when deciding the appropriate action level, which should be used for the IGRT technique.

**Pre-Treatment Imaging**

For palliative lung RT, a CT planning scan is highly recommended. For radical lung RT CT planning is required with IV contrast recommended for all lesions close or involving the mediastinum (including nodal disease) and for those tumours close to the brachial plexus. PET/CT fusion is recommended to help GTV delineation and identify tumour from lung collapse.

**On-Treatment Imaging**

For palliative treatments with large margins, planar imaging matching to a bony surrogate is acceptable, though volumetric imaging is preferable if available as soft tissue target.

For palliative treatments ≤ 5 fractions a single day 0/1 check is the minimum required. Further imaging may be required if there is a gross error or large shift (e.g. >1cm) required at fraction 1 or there are concerns regarding reproducibility for subsequent treatments.

For palliative treatments that are > 5 fractions the offline error reduction protocol should be used with repeat imaging weekly to detect changes.

For the vast majority of ***radically*** treated lung tumours, volumetric imaging with cone beam CT, CT on rails or megavoltage CT is highly recommended as bony landmarks are not a reliable surrogate and can detect changes in internal anatomy. In certain circumstances planar imaging is acceptable for all fractions i.e. paraveterbral or Pancoast's tumours where bone is a reliable surrogate for tumour position. For some central tumours where the carina may be an adequate surrogate for the tumour position, planar imaging may acceptable perform a match to the carina[4]. However, the lung may re-inflate during the RT course and this is easier to detect with volumetric imaging. For standard conventional fractionation schedules, i.e. 20-33 fractions, using conventional larger margins the offline systematic error reduction protocol should be used. If margin reduction is to be considered more frequent imaging is required to reduce the random and changes in the systematic error over the treatment course [5.6]. For more hypofractionated regimes, e.g. SABR, daily online imaging matching to the target or fiducial is mandatory.

**Site Specific Issues:** Re-planning may be required for conventional fractionation treatments. Each individual centre will need to consider an appropriate action for re-planning based on their current resources and this needs to be decided with the clinical oncologist and medical physics team.

When considering more complex radiotherapy including, IMRT, concomitant RT boost or margin reduction, the online random error reduction protocol should be used. Ideally, this should be done in the context of previous experience and assessments, a clinical trial or prospective institutional audit, so that the set-up results are analysed and used to verify the adequacy of the PTV margin and appropriateness of the imaging technique (anatomy reviewed, frequency and action levels).

For these more complex RT techniques imaging of the target with volumetric imaging or matching to implanted fiducials is mandatory.

Fiducials, both external and internal, can be used for tracking intra-fraction motion and gating. Both require specialist equipment. Gating with external surrogates needs to be carefully assessed, as tumour motion may not correlate with external anatomy[7]. In addition, if fiducials are to be used to match, we would recommend using further (ideally volumetric) imaging to check the position of the fiducials and monitor for changes in the internal anatomy during a radiotherapy course.

For extreme hypofractionated radiotherapy e.g. SABR, daily imaging matching to the target or implanted fiducials using the online error pathway is mandatory. For CBCT based SBRT multiple images during the treatment fraction can be considered to verify any shift or if the treatment exceeds 30 minutes[8].

If available, monitoring for intra-fraction changes with fluoroscopy, implanted fiducials or surface anatomy tracking can be used.

**References:**


1. Steenbakkers RJ, Duppen JC, Fitton I, Deurloo KE, Zijp L, Uitterhoeve AL, Rodrigus PT, Kramer GW, Bussink J, De Jaeger K, Belderbos JS, Hart AA, Nowak PJ, van Herk M, Rasch CR. Observer variation in target volume delineation of lung cancer related to radiation oncologist-computer interaction: a 'Big Brother' evaluation. Radiother Oncol. 2005 Nov;77(2):182-90. Epub 2005 Oct 26. PubMed
2. PMID: 16256231.

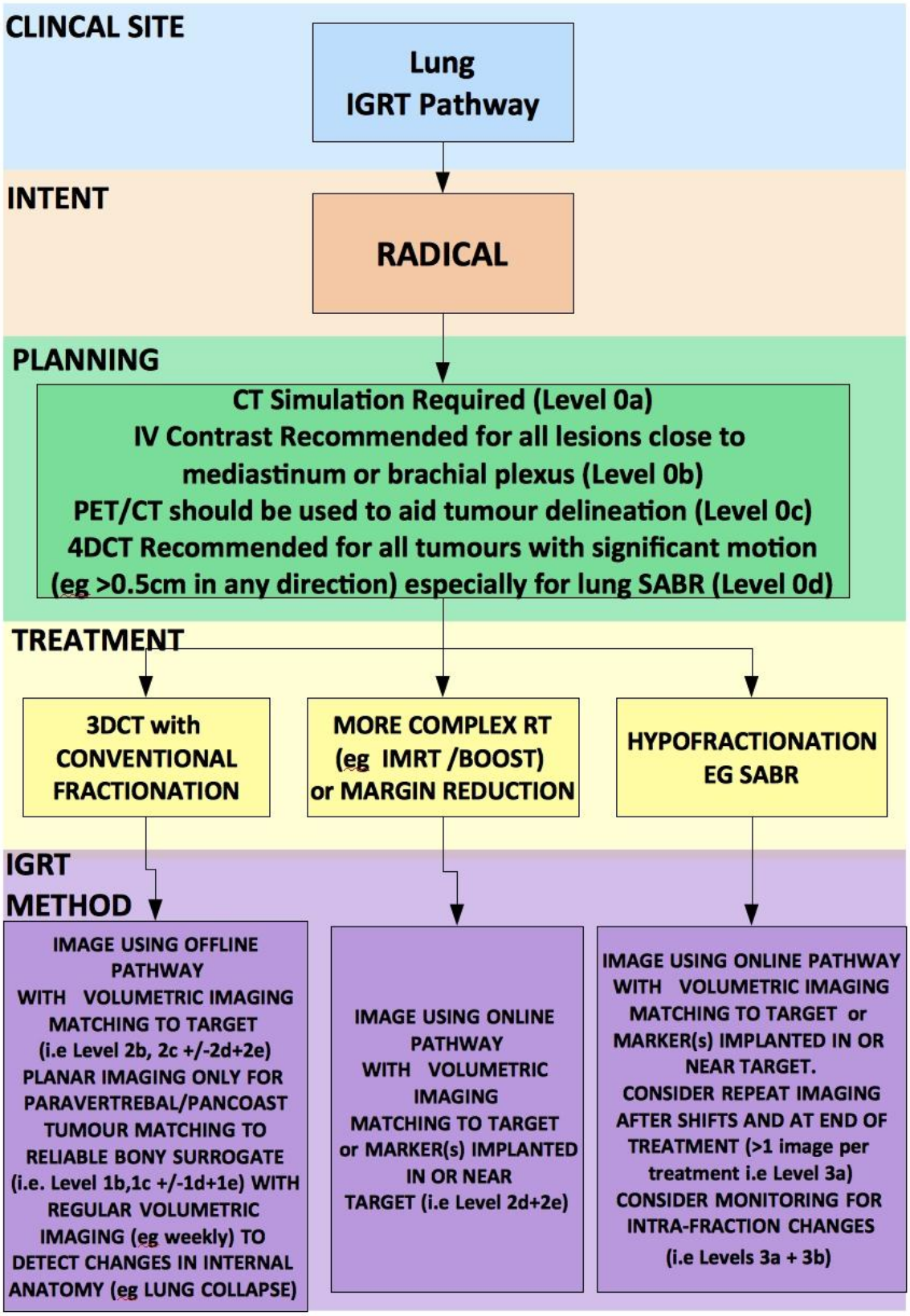
3. Hanna GG, McAleese J, Carson KJ, Stewart DP, Cosgrove VP, Eakin RL, Zatari A, Lynch T, Jarritt PH, Young VA, O'Sullivan JM, Hounsell AR. (18)F-FDG PET-CT simulation for non-small-cell lung cancer: effect in patients already staged by PET-CT. Int J Radiat Oncol Biol Phys. 2010 May 1;77(1):24-30. Epub 2009 Aug 6. PubMed PMID: 19665324.
4. Shirato H, Seppenwoolde Y, Kitamura K, Onimura R, Shimizu S. Intrafractional tumor motion: lung and liver. Semin Radiat Oncol. 2004 Jan;14(1):10-8. PubMed PMID: 14752729.

5. Higgins J, Bezjak A, Franks K, Le LW, Cho BC, Payne D, Bissonnette JP. Comparison of spine, carina, and tumor as registration landmarks for volumetric image-guided lung radiotherapy. Int J Radiat Oncol Biol Phys. 2009 Apr 1;73(5):1404-13. Epub 2008 Sep 17. PubMed PMID: 18804335.

6. Higgins J, Bezjak A, Hope A, Panzarella T, Li W, Cho JB, Craig T, Brade A, Sun A, Bissonnette JP. Effect of image-guidance frequency on geometric accuracy and setup margins in radiotherapy for locally advanced lung cancer. Int J Radiat Oncol Biol Phys. 2011 Aug 1;80(5):1330-7. Epub 2010 Jul 17. PubMed PMID: 20643515.

7. Hoisak JD, Sixel KE, Tirona R, Cheung PC, Pignol JP. Correlation of lung tumor motion with external surrogate indicators of respiration. Int J Radiat Oncol Biol Phys. 2004 Nov 15;60(4):1298-306. PubMed PMID: 15519803.

8. Purdie TG, Bissonnette JP, Franks K, Bezjak A, Payne D, Sie F, Sharpe MB, Jaffray DA. Cone-beam computed tomography for on-line image guidance of lung stereotactic radiotherapy: localization, verification, and intrafraction tumor position. Int J Radiat Oncol Biol Phys. 2007 May 1;68(1):243-52. Epub 2007 Feb PubMed PMID: 17331671.


CLINCAL SITE
Lung
IGRT Pathway
INTENT
RADICAL
PLANNING
CT Simulation Required (Level 0a)
IV Contrast Recommended for all lesions close to mediastinum or brachial plexus (Level 0b)
PET/CT should be used to aid tumour delineation (Level 0c)
4DCT Recommended for all tumours with significant motion (eg >0.5cm in any direction) especially for lung SABR (Level 0d)
TREATMENT
3DCT with CONVENTIONAL FRACTIONATION
MORE COMPLEX RT (eg IMRT /BOOST) or MARGIN REDUCTION
HYPOFRACTIONATION EG SABR
IGRT METHOD
IMAGE USING OFFLINE PATHWAY WITH VOLUMETRIC IMAGING MATCHING TO TARGET (i.e Level 2b, 2c +/-2d+2e) PLANAR IMAGING ONLY FOR PARAVERTREBAL/PANCOAST TUMOUR MATCHING TO RELIABLE BONY SURROGATE (i.e. Level 1b,1c +/-1d+1e) WITH REGULAR VOLUMETRIC IMAGING (eg weekly) TO DETECT CHANGES IN INTERNAL ANATOMY (eg LUNG COLLAPSE)
IMAGE USING ONLINE PATHWAY WITH VOLUMETRIC IMAGING MATCHING TO TARGET or MARKER(s) IMPLANTED IN OR NEAR TARGET (i.e Level 2d+2e)
IMAGE USING ONLINE PATHWAY WITH VOLUMETRIC IMAGING MATCHING TO TARGET or MARKER(s) IMPLANTED IN OR NEAR TARGET. CONSIDER REPEAT IMAGING AFTER SHIFTS AND AT END OF TREATMENT (>1 image per treatment i.e Level 3a) CONSIDER MONITORING FOR INTRA-FRACTION CHANGES (i.e Levels 3a + 3b)

## Urological

### Bladder

**Background:** Bony imaging only is inadequate because bladder organ motion, mainly due to volume changes, occurs independently to bony anatomy and can cause large variations in the shape and position of the bladder, leading to geographical miss[1]. Furthermore, changes in rectal filling may lead to positional, but not conformational, changes[2,3].

**Immobilisation and reproducibility:** Patient positioning should be comfortable and reproducible to ensure stability. Immobilisation devices generally consist of a knee cushion and ankle support. A consistent bladder volume is important and catheterisation throughout planning and treatment in patients with a large residual bladder volume.

The use of written patient information about bladder filling or emptying should be considered. Attention should also be paid to rectal volume and enema and/or laxatives should be used in patients with large rectal volume at initial planning scan.

Pre treatment imaging: CT slice thickness should be 3-5mm with IV contrast used if treating whole pelvis.

Conventionally, relatively large population-based isotropic margins of 15-20 mm are applied to the CTV (whole bladder) to avoid geographical miss, but this may be a suboptimal approach for many patients because excessive normal tissue is irradiated in those with smaller variations in position or conversely geographical miss may occur in those with larger variations

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)[4-6]. This strongly argues for the use of anisotropic margins for internal organ motion.

**On treatment imaging:** High quality volumetric imaging such as ultrasound, CT and on-treatment CBCT are usually able to give sufficient resolution to visualise the bladder and rectum.

For standard CTV to PTV margins of 15-20mm volumetric imaging should be used for the first 3 to 5 fractions to identify and correct for systematic errors (off-line protocol). Up to 25% of patients may have a systematic change in bladder size and/or shape and will require re-planning[4].

In patients displaying significant random errors or treated with smaller margins daily on-line volumetric imaging will be required to reduce the risk of geographical miss.

**Specific issues:** Inter- and intra-fraction volume changes lead to shape changes rather than a three-dimensional vector displacement of a stable volume. A number of more complex IGRT, i.e. adaptive, solutions have been suggested and are currently under evaluation in the research setting. These include: -

(i) Use of 'PTV of the day'[4] a technique requiring multiple approved PTVs and plans, corresponding to variable superior CTV to PTV margins. Volumetric imaging is used to select the most appropriate plan. Planning studies suggest the main benefit would be sparing of small bowel.

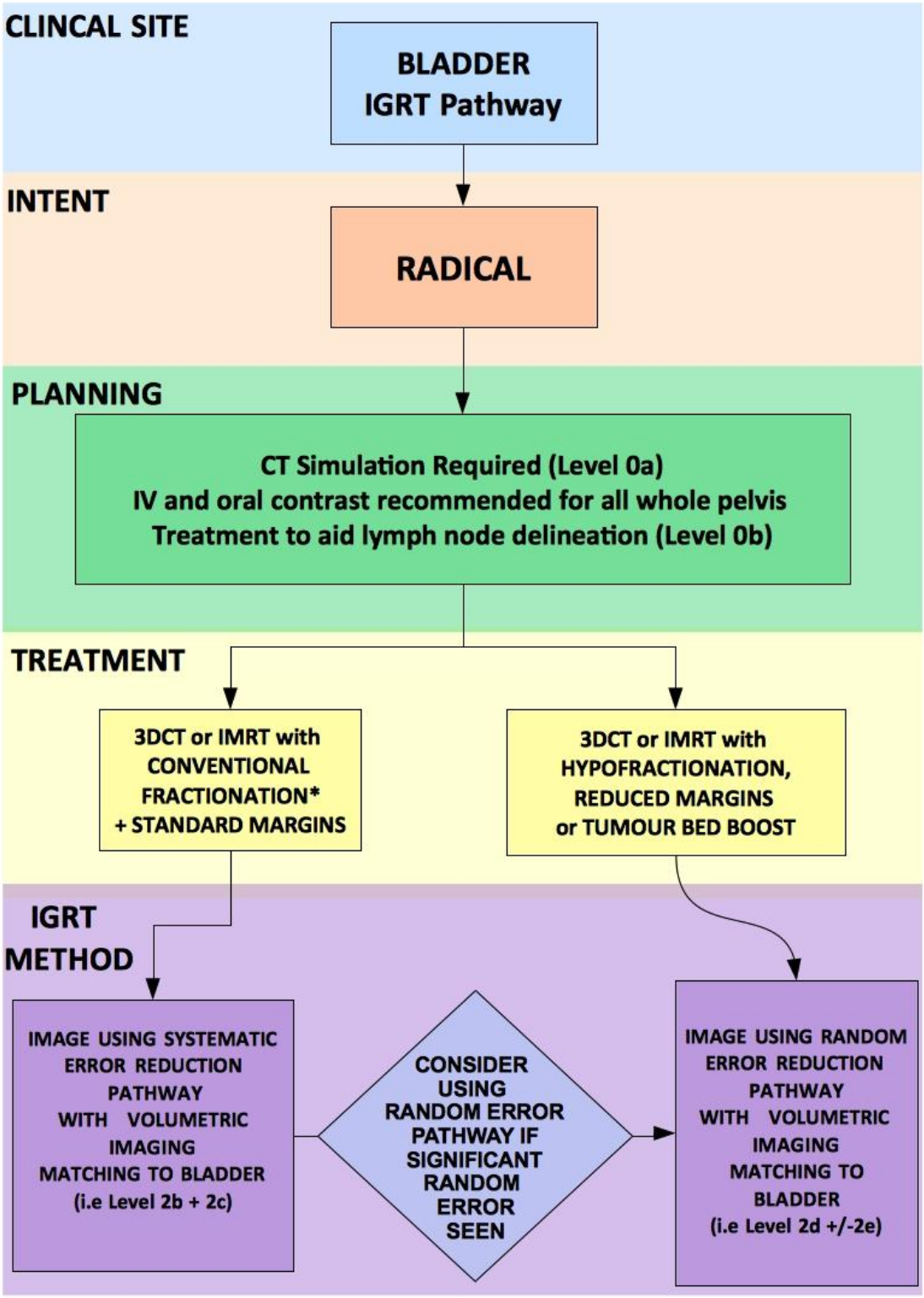
(ii) Adaptive predictive organ localisation (A-POLO) where the daily target volume and plan is selected individually using a model based on the patient's three-dimensional bladder filling pattern, which is applied to a daily pre-treatment CBCT. The added benefit of A-POLO over 'PTV of the day' is incorporation of the volume changes from bladder filling during the online process.

(iii) Processing of the CBCT image[7] a technique where during the first week of treatment, multiple CBCT images are acquired and used to define an individualised composite GTV by defining the maximal volume on each slice[8-9]. An adaptive PTV is then generated and used for the remainder of the treatment course with CBCT used to confirm delivery accuracy.

(iv) Fiducial markers and cystoscopically inserted lipiodol have been used in the research setting for IGRT and may be particularly helpful when using partial bladder radiotherapy or focal boost.

**References:**


1. Harris SJ, Buchanan RB. An audit and evaluation of bladder movements during radical radiotherapy. Clin Oncol 1998;10 (4):262e264.
2. Pos FJ, Hulshof M, Lebesque J, et al. Adaptive radiotherapy for invasive bladder cancer: a feasibility study. Int J Radiat Oncol Biol Phys 2006;64(3):862e868.
3. Lotz HT, Remeijer P, van Herk M, et al. A model to predict bladder shapes from changes in bladder and rectal filling. Med Phys 2004;31(6):1415e1423.
4. Burridge N, Amer A, Marchant T, et al. Online adaptive radiotherapy of the bladder: small bowel irradiated-volume reduction. Int J Radiat Oncol Biol Phys 2006;66(3):892e897.
5. Meijer GJ, Rasch C, Remeijer P, Lebesque JV. Three-dimensional analysis of delineation errors, setup errors, and organ motion during radiotherapy of bladder cancer. Int J Radiat Oncol Biol Phys 2003;55(5):1277e1287.
6. Muren LP, Smaaland R, Dahl O. Organ motion, set-up variation and treatment margins in radical radiotherapy of urinary bladder cancer. Radiother Oncol 2003;69(3):291e304.
7. Lalondrelle S, Huddart R. Improving radiotherapy for bladder cancer: an opportunity to integrate new technologies. Clin Oncol 2009;21(5):380e384.
8. Pos FJ, van Tienhoven G, Hulshof MC, Koedooder K, Gonzalez Gonzalez D. Concomitant boost radiotherapy for muscle invasive bladder cancer. Radiother Oncol 2003;68 (1):75e80.
9. Foroudi F, Wong J, Haworth A, et al. Offline adaptive radiotherapy for bladder cancer using cone beam computed tomography. J Med Imaging Radiat Oncol 2009;53(2): 226e233.




* Includes moderately hypofractionated regimes e.g. 55Gy/20fr

## Prostate

**Background:** Prostate motion, independent of bony anatomy, has often been demonstrated during a course of radiotherapy treatment and there is clear evidence that IGRT is essential both to reduce the risk of geographical miss and minimise toxicity[1]. Therefore for accurate targeting, the prostate must be imaged directly using volumetric imaging or a surrogate such as implanted prostate markers.

Acute toxicity has been shown to be reduced in a single centre using prostate marker based daily IGRT compared to bone matched treatments[2]. It is hoped that a reduction in acute bowel and bladder toxicity will translate into a reduced rate of consequential late damage. However, inappropriately small margins when using daily IGRT have been shown to result in higher relapse rates[3].

**Immobilisation and reproducibility**: Patient positioning should include a knee cushion and ankle support. Fixation of the ankles is particularly important because a combination of leg scissor movement and leg roll had the most significant influence on prostate rotation[4].

To achieve a reproducible pelvic treatment set-up a reliable method of setting the isocentre is essential. By using the couch height rather than skin marks a more reproducible baseline set-up in the anterior-posterior direction was shown to be achieved, prior to any imaging[5].

Patient preparation in particular, attention to rectal volume both at planning and during treatment delivery is important. Patients whose initial CT scan shows the largest rectal volume have been shown to have the greatest decrease in rectal volume during treatment[6] and also to have a poorer treatment outcome[7,8]. A minimum requirement should include a departmental protocol and patient information sheet that ensures consistent practice at planning and during treatment delivery. For example rectal volume at planning scan can be assessed with a pre-defined cut-off (e.g. 4cm AP diameter and 3 cm lateral diameter) and intervention used (enema and/or laxatives) if exceeded. Approximately 20% of patients needed repeat planning CT to reduce rectal volume[8].

**Pre Treatment imaging:** CT slice thickness should be <3mm. CT/MRI fusion is recommended to aid prostate delineation

IV contrast should be used if treating whole pelvis to assist in outlining the nodal target.

**On treatment imaging:** Target imaging (prostate markers or volumetric imaging) to exclude large systematic errors due to residual bladder/rectal changes at least days 1-3 and weekly is mandated.

The additional benefit of online vs. offline target based IGRT is uncertain when using UK standard margins of the order of 10mm[9]. However if margins are reduced, daily IGRT may be necessary to minimise the risk of geographical miss due to inter-fraction random changes in prostate position. When reducing margins and using on line imaging the effect of intra fraction motion and rotations must still be considered[10,11].

The use of markers offers increased accuracy with minimal dose implication and little time penalty depending on the equipment available for example if using kV imaging and automatic couch correction the additional time is 2 minutes[12]. If non-automatic couch repositioning is used then

post-correction images must be taken to ensure the correction has been applied in the right direction.

Although imaging technology is constantly improving the image quality of prostate cone beam CT can make accurate matching difficult and considerable inter-observer variability has been demonstrated in defining the prostate and surrounding tissues[13]. More clinician input and/or training may be required compared to marker matching and the impact of observer variability should be accounted for when margin reduction using cone beam CT IGRT is considered. However volumetric imaging can detect prostate motion as well as bladder and rectum position and shape. Intervention can then be used if required for example improved patient information or allowing the patient time to empty rectum/pass gas.

More advanced concepts in prostate radiotherapy such as extreme hypofractionation/SABR and sub-volume boosting based on functional imaging/template biopsies will require a higher level of positional accuracy and therefore daily online IGRT +/- intrafractional error correction are recommended.

**Site specific issues**: Re-planning may be required during treatment if systematic errors due to rotations, not easily corrected for by couch shift, or seminal vesicle deformation are noted. If seminal vesicle coverage is important, then volumetric imaging in addition or in lieu of prostate markers is preferred. Random errors due to rotations or deformation may require larger CTV to PTV margins and on-line IGRT.

Functional MRI/template biopsy should be considered if delivering a boost to a dominant intraprostatic lesion.

**Whole pelvis treatments and post-operative patients**

In patients treated with whole pelvic irradiation and a prostate boost it is generally assumed that the main OAR is the rectum and target matching to the prostate therefore takes priority to bone matching for pelvic lymph node verification. Differential CTV to PTV margins should be used to take account of this i.e. larger margins for the whole pelvic treatment.

In post-operative patients, organ motion is generally less significant. As markers are difficult to place, volumetric imaging is preferred.

**References:**


1. Button MR, Staffurth JN. Clinical application of Image-guided radiotherapy in bladder and prostate cancer. Clinical Oncology 2010; 22: 698-706.
2. Gill S, Thomas J, Fox C, et al. Acute toxicity in prostate cancer patients treated with and without image-guided radiotherapy. Radiation Oncology 2011; 6: 145.
3. Engels B, Soete G, Verellen D, Storme G. Conformal arc radiotherapy for prostate cancer: increased biochemical failure in patients with distended rectum on the planning computed tomogram despite image guidance by implanted markers.Int J Radiat Oncol Biol Phys. 2009 Jun 1;74(2):388-91
4. Van Herk, M, Bruce, A, Kroes, AP, et al, 1995; Quantification of organ motion during conformal radiotherapy of the prostate by three dimensional image registration; Int J Radiat Oncol Biol Phys; 33, 1311-1320.

5. Van Lin, EN, Nijenhuis, E, Huizenga, H, et al, 2001; Effectiveness of couch height-based patient set-up and an off-line correction protocol in prostate cancer radiotherapy; Int J Radiat Oncol Biol Phys; 50, 569-577.

6. Pinkawa, M, Siluschek, J, Gagel, B, et al, 2006; Influence of the initial rectal distension on posterior margins in primary and postoperative radiotherapy for prostate cancer; Radiother Oncol; 81, 284-290.

7. de Crevoisier R, Tucker SL, Dong L, et al. Increased risk of biochemical and local failure in patients with distended rectum on the planning CT for prostate cancer radiotherapy. Int J Radiat Oncol Biol Phys 2005;62:965–973.

8. Stillie AL, Kron T, Fox C et al. Rectal filling at planning does not predict stability of the prostate gland during a course of radical radiotherapy if patients with a large rectum are re-imaged. Clin Oncol 2009; 21, 760-767.

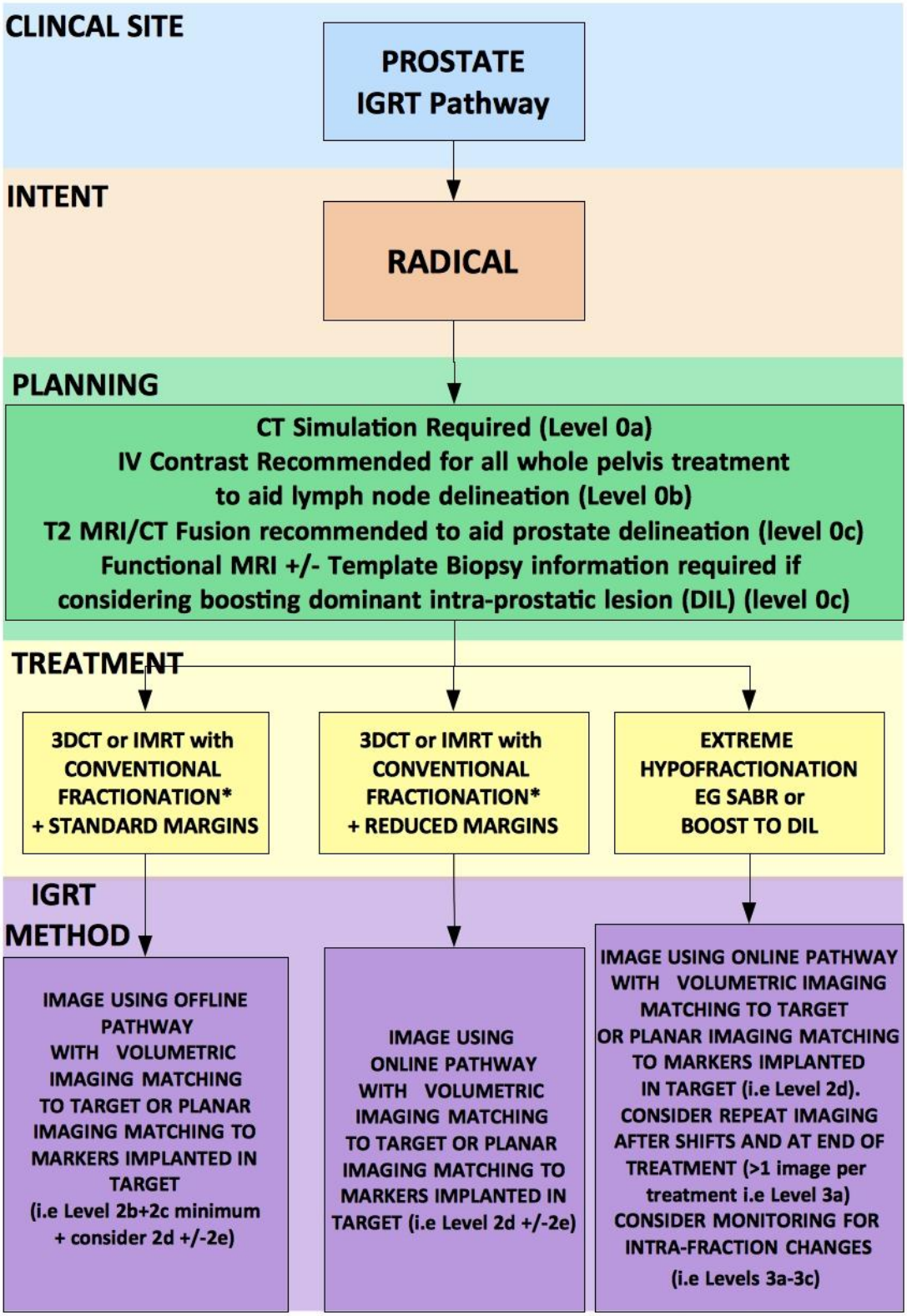
9. McNair HA, Hansen VN, Parker CR, et al. Comparison of the use of bony anatomy and internal markers for offline verification and an evaluation of the potential benefit of online and offline verification protocols for prostate radiotherapy. Int J Radiat Oncol Biol Phys 2008; 71, 41-50.

10. Langen KM, Shah AP, Willoughby TR, et al. Real-time position adjustment during treatment for localized prostate cancer: observations on clinical use and acute toxicity. Int J Radiat Oncol Biol Phys 2009: 75(3): S2252.

11. Lips IM, van der Heide UA, Kotte AN, van Vulpen M, Bel A. Effect of translational and rotational errors on complex dose distributions with off-line and on-line position verification. Int J Radiat Oncol Biol Phys. 2009 Aug 1;74(5):1600-8

12. Baker A, Fenwick JD, Mayles WP, et al. A comparison of imaging schedules for prostate radiotherapy including online tracking techniques. Journal of Radiotherapy in Practice 2011; 10:239-49.

13. Barney BM, Lee RJ, Handrahan D, et al. Image-guided Radiotherapy (IGRT) for prostate cancer comparing kV imaging of fiducial markers with cone beam computed tomography. Int J Radiat Oncol Biol Phys 2011; 80:301-5.




* Includes moderately hypofractionated regimes e.g. 57Gy/19fr

**Appendix I**

## NRIG – Image Guided Radiotherapy sub-group terms of reference

**Purpose**

To support the uptake and appropriate (evidence-based) use of Treatment Delivery Image-Guided Radiotherapy (IGRT) in Radiotherapy Centres in England. This will be achieved by providing guidance for radiotherapy professionals in implementing good IGRT practices and information for managers for commissioning IGRT services.

**Background**

These guidelines aim to contribute to the strategy for developing and improving radiotherapy services in England, as recommended by the National Radiotherapy Advisory Group (NRAG) technology subgroup report. They expand on the recommendations from the RCR/SCoR/IPEM document, 'On-Target: ensuring geometric accuracy in radiotherapy' and take this work forwards.

**Terms of reference**

- The group should liaise with clinical service experts, the Department of Health and National Cancer Action Team to scope and understand the role of IGRT.
- The group will focus on key areas:
  1. Process of IGRT methodology and technology
  2. Process of Image review which reflects the varying levels of complexity. This includes cross speciality training with competency assessments.
  3. Data collection
  4. Image quality
  5. Recommendations of implementation
  6. Trials and future use
- The group will consider and collate the clinical evidence for potential to improve the quality of radiotherapy using these technologies.
- The group will consider image review and training. It will consider setting standards for review and recommendations for training
- The group will work to provide a framework for IGRT provision, and set this in the context of the current commissioning profile to support commissioner understanding.
- The group will report progress and finding to NRIG on a regular basis; and a final report no later than 12 months following the group's first meeting.

**Frequency**

This will be a short-life working group; meeting approximately 4 times over one year; with much work being undertaken by e-mail and telephone conference if possible.

**Appendix II**

**Membership of the IGRT Group and contributors to the report (*)**

| NAME | JOB TITLE | ORGANISATION |
|---|---|---|
| Kevin Franks (co-Chair) | Consultant Clinical Oncologist | St James's Institute of Oncology, Leeds |
| Helen McNair (co-Chair) | Research Radiographer | The Royal Marsden NHS Foundation Trust |
| Angela Baker | Research Radiographer | Clatterbridge Centre for Oncology |
| Úna Findlay | Senior Clinical Radiotherapy Officer | Health Protection Agency |
| Charlotte Beardmore | Professional Officer | Society & College of Radiographers |
| Neil Burnet | Consultant and Reader in Clinical Oncology | Addenbrooke's Hospital Cambridge |
| Katherine Burton* | Consultant Radiographer | Addenbrooke's Hospital Cambridge |
| Catharine Clark | Consultant Physicist | Royal Surrey Hospital / National Physical Laboratory |
| Charlotte Coles* | Consultant Clinical Oncologist | Addenbrookes Hospital Cambridge |
| Rachael Cooper | Consultant Clinical Oncologist | St James's Institute of Oncology, Leeds |
| Tim Cooper | Associate Director, Radiotherapy | National Cancer Action Team |
| Adrian Crellin* | Dean RCR<br>Consultant Clinical Oncologist | Royal College of Radiologists |
| June Dean* | National IGRT Training Lead | National Cancer Action Team / SCoR |
| Ellen Donovan | NIHR Post-Doctoral Research Fellow | The Royal Marsden NHS Foundation Trust |
| Diane Eden | Commissioner | Cumbria and Lancashire Business Service |
| Mark Elsworthy* | National IGRT Training Lead | National Cancer Action Team / SCoR |
| Corrine Faivre-Finn* | Consultant Clinical Oncologist | The Christie Hospital |
| Russell Hart | Radiotherapy Services Manager | Nottingham University Hospitals NHS Trust |
| Maria Hawkins | Consultant Clinical Oncologist | The Royal Marsden NHS Foundation Trust |
| Ann Henry | Consultant Clinical Oncologist | St James's Institute of Oncology, Leeds |
| Peter Kirkbride | National Advisor Radiotherapy Improvement<br>Consultant Clinical Oncologist | National Cancer Action Team<br>Weston Park Hospital, Sheffield |
| Elizabeth Miles | National Trials QA Team Co-ordinator | Mount Vernon Hospital |
| Christopher Nutting* | Consultant and Reader in Clinical Oncology | The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research |
| Donna Routsis | Research Radiographer | Addenbrooke's Hospital Cambridge |
| John Pettingell | Consultant Physicist | Cancer Partners UK |
| Melanie Powell | Consultant Clinical Oncologist | Barts and the London |
| Andrew Reilly | Consultant Physicist | Clatterbridge Centre for Oncology |
| Christopher Scrase | Macmillan Consultant Clinical Oncologist | The Ipswich Hospital NHS Trust |
| Julie Stratford | Research Radiographer | The Christie Hospital |
| Jonathan Sykes | Consultant Physicist | St James's Institute of Oncology, Leeds |
| Linda Samuels | Lay Representative | National Radiotherapy Implementation Group |
| John Staffurth | Consultant Clinical Oncologist | Velindre Hospital Wales |
| Michael Williams | Consultant Clinical Oncologist<br>Chair NRIG | Addenbrooke's Hospital Cambridge |

**Appendix III**

**Abbreviations**

| | |
|---|---|
| **CBCT** | **Cone Beam CT** |
| **CTV** | **Clinical Target Volume** |
| **DRR** | **Digitally Reconstructed Radiograph** |
| **Gy** | **Gray – a unit of radiation dose measurement** |
| **IGRT** | **Image Guided Radiotherapy** |
| **IMRT** | **Intensity Modulated Radiotherapy** |
| **IPEM** | **Institute of Physics and Engineering in Medicine** |
| **ITV** | **Internal Target Volume** |
| **MLC** | **Multileaf Collimator** |
| **MV** | **Megavoltage** |
| **MU** | **Monitor Units** |
| **NRAG** | **National Radiotherapy Advisory Group** |
| **NRIG** | **National Radiotherapy Implementation Group** |
| **PTV** | **Planning Target Volume** |
| **QA** | **Quality Assurance** |
| **RCR** | **Royal College of Radiologists** |
| **SBRT** | **Stereotactic Body Radiotherapy** |
| **SRS** | **Stereotactic radiosurgery** |
| **SRT** | **Stereotactic Radiotherapy** |
| **TPS** | **Treatment Planning System** |

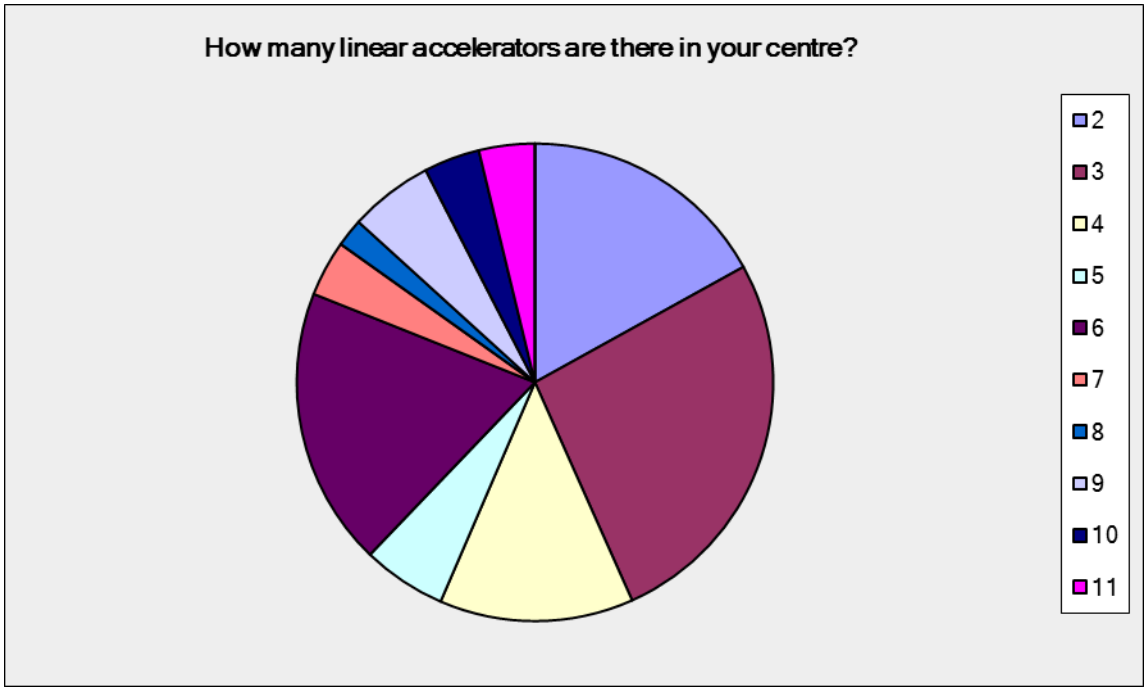
A**ppendix IV**

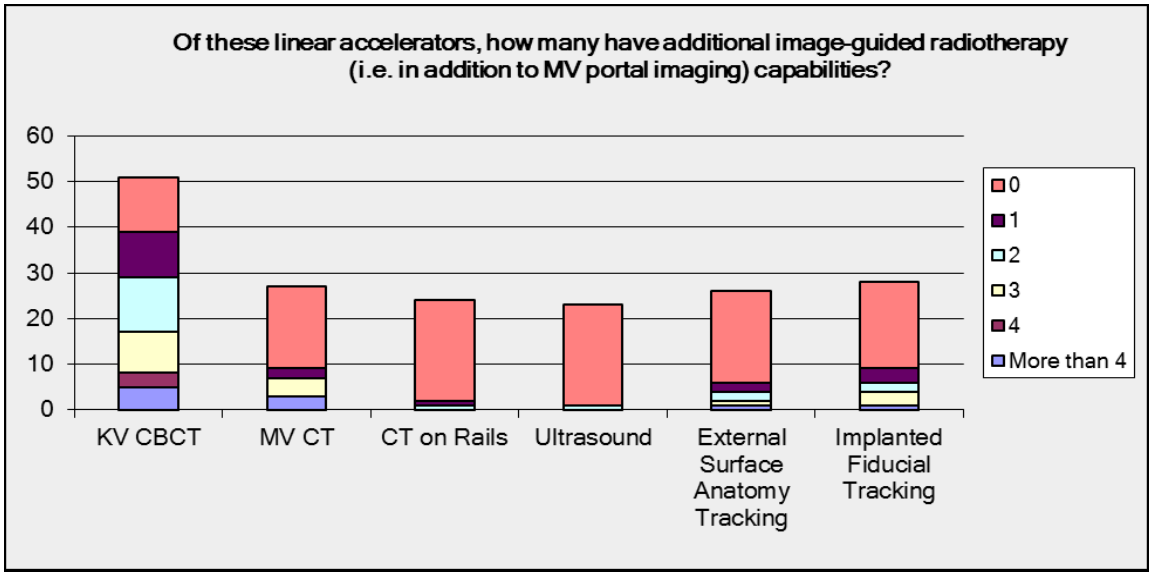
**IGRT Survey Data**

During Summer 2011, a survey of IGRT use and availability was conducted.

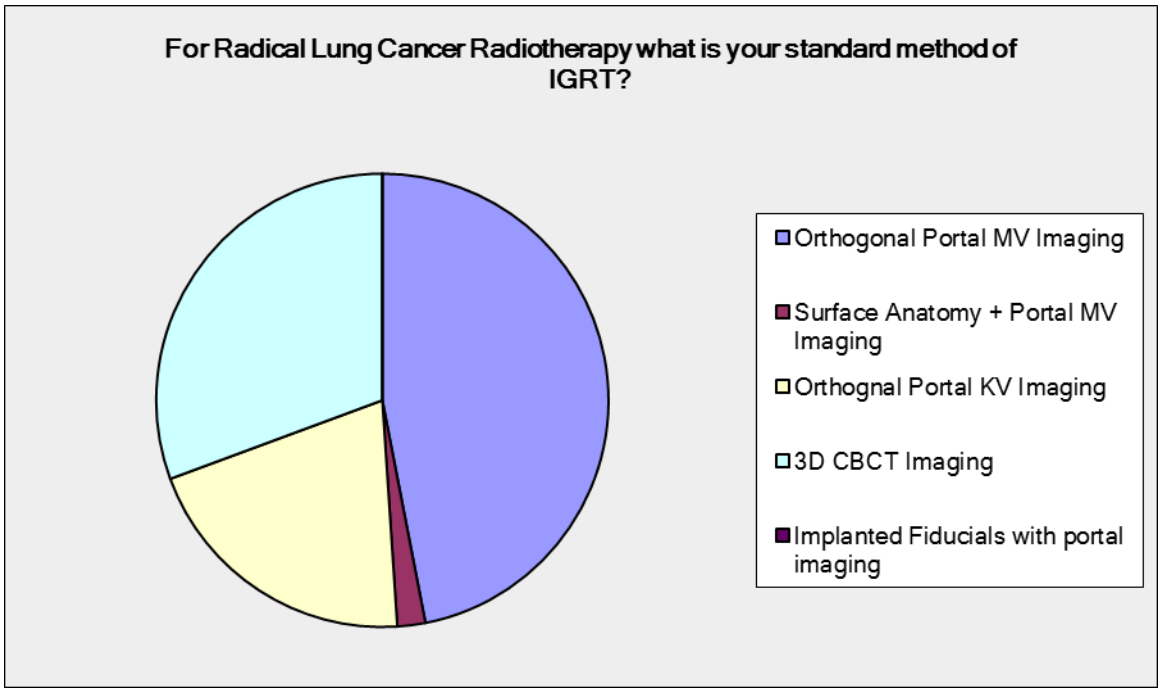
A total of 55 responses were received from a large range of services

The responses to key questions are reproduced below

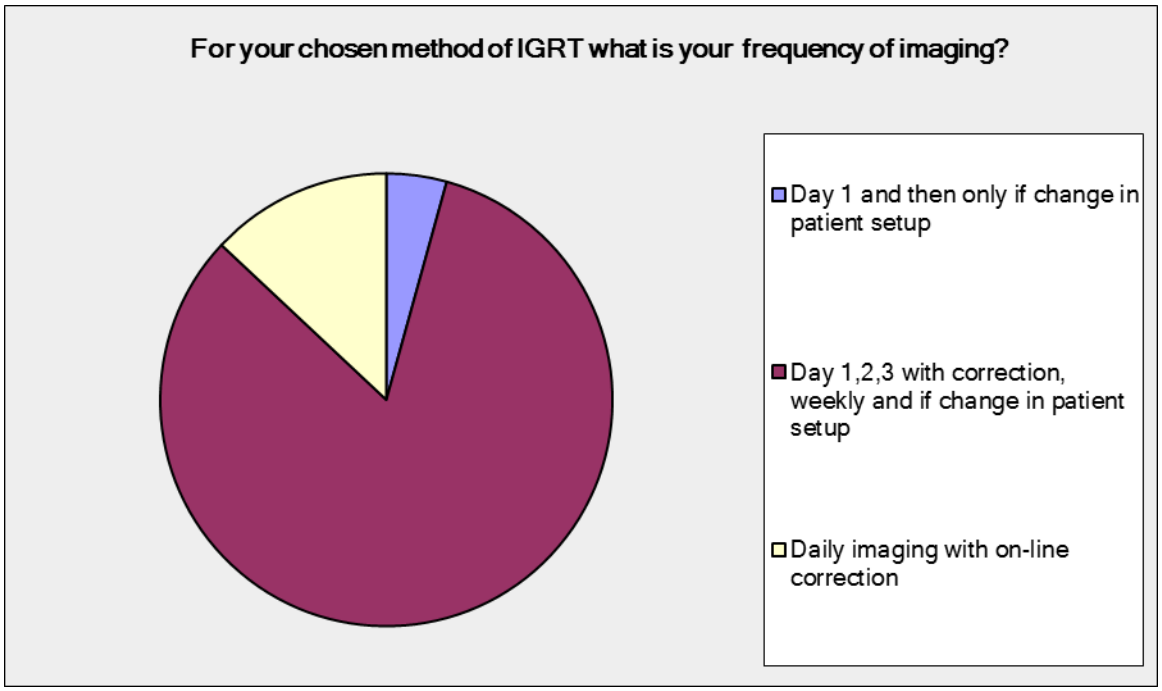


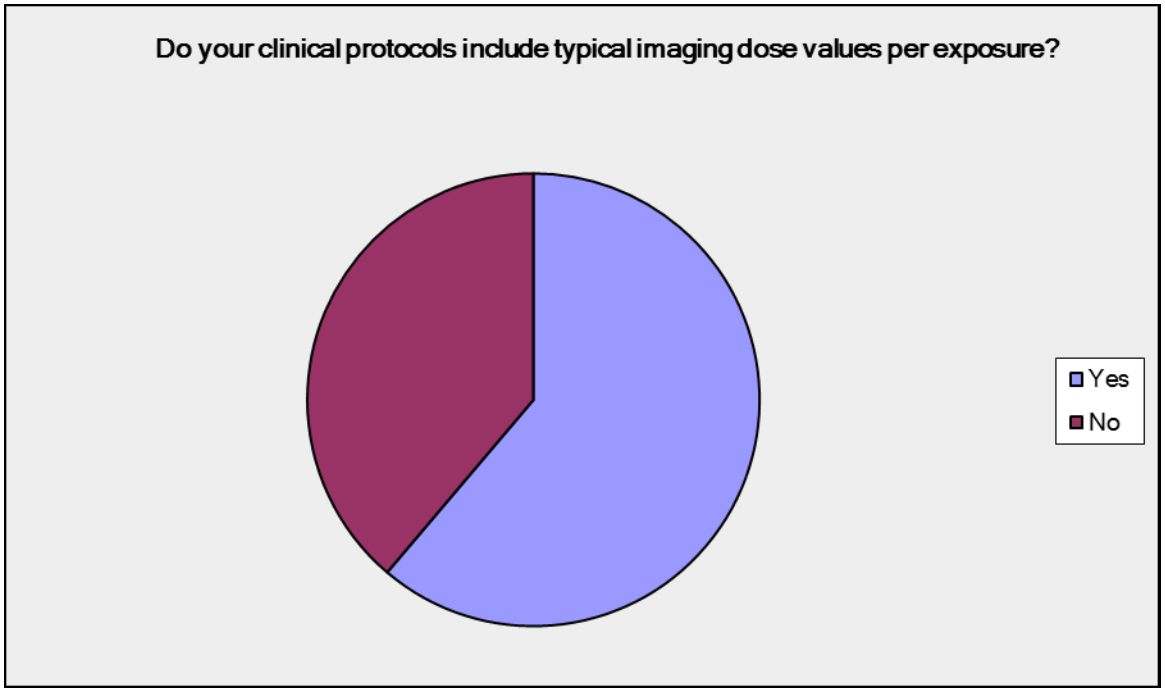
Using Lung as an example, the results indication that nationally, orthogonal portal MV imaging is the most used method in radiotherapy services.



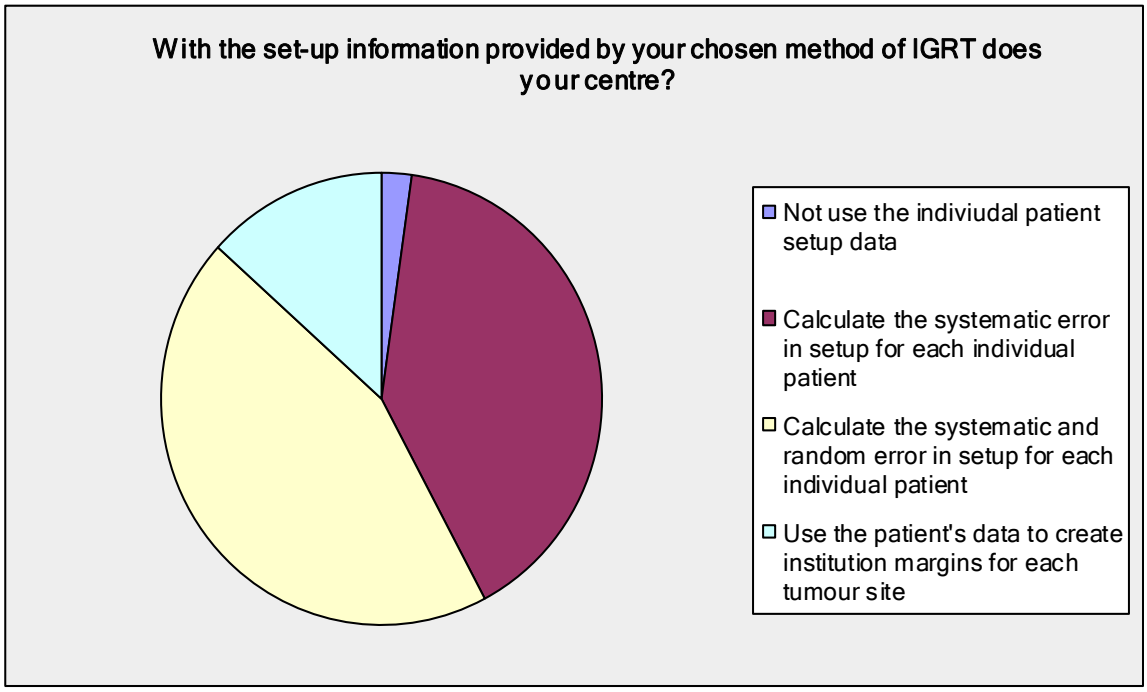

Equally the results indicate the main frequency is on day 1,2 and 3 with correction; and subsequent imaging weekly or if a change in patients set-up



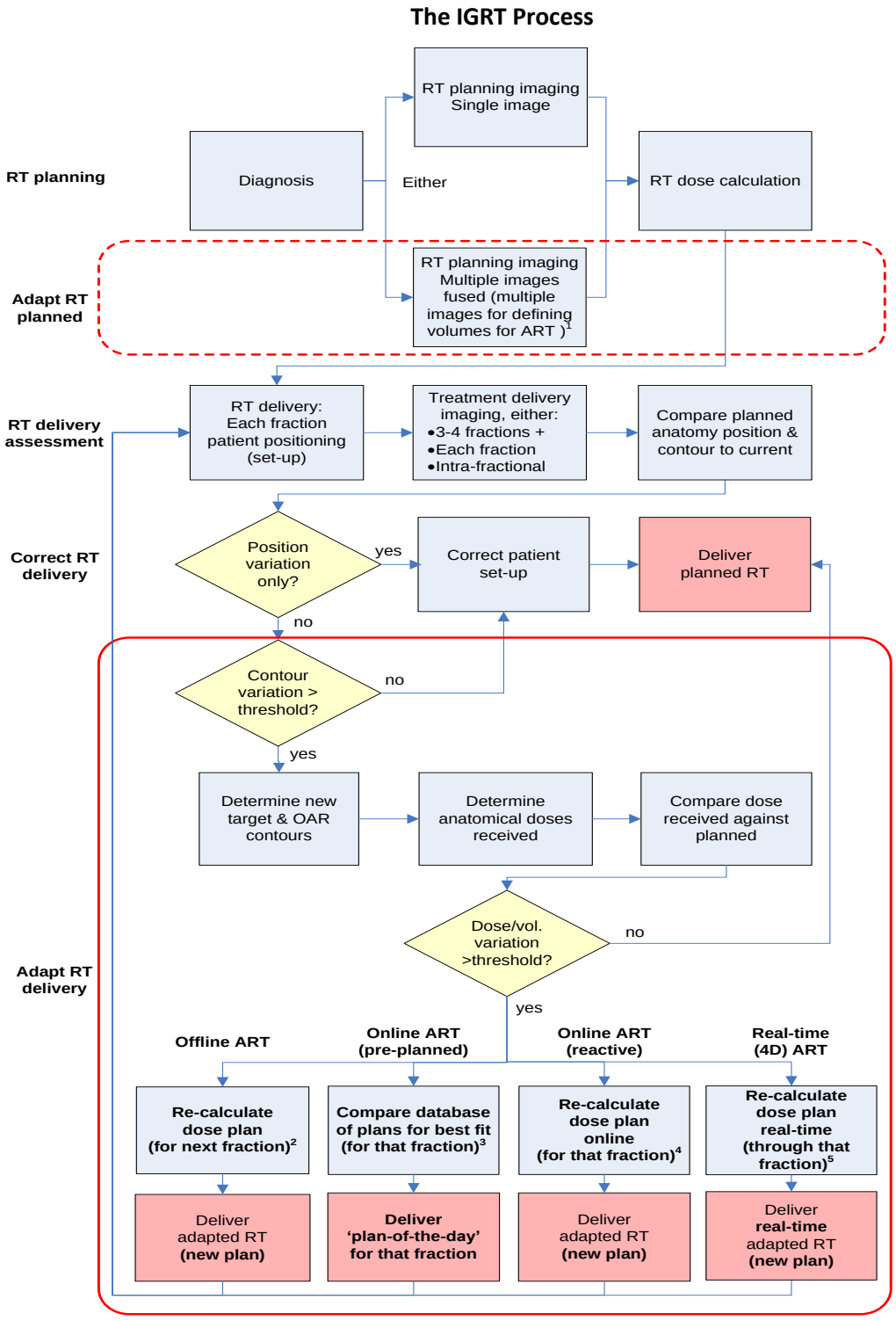
When asked about use of protocols, almost 40% did not specify imaging dose.




Over half of all centres did not calculate individual random error for patients.



## Appendix V




[1] Evans 2008
[2] Martinez 2001
[3] Tuomikoski 2011
[4] Mackie 1999
[5] Pos 2006

A**ppendix VI**

Example of image risk assessment

| **IGRT Process** | **Description of risk** | **What factors may cause this risk to occur** | **Existing control measures for each potential hazard** | **Risk Level (1 low -5 high)** |
|---|---|---|---|---|
| **Acquisition** | Gantry collision with patient | Off set isocentre | Safety check for gantry clearance before each acquisition | 3 |
| | Treated with Incorrect isocentre | Isocentre has to be moved for CBCT | Record and verify system | 3 |
| **Analysis process** | Anatomy changes missed | Lack of training/awareness | Training | 4 |
| | Potential for geographical miss if on line matching | Lack of training | Training<br>Clinician to be present if staff not trained to advanced level | 4 |
| | Incorrect target surrogate i.e. seed outlined | Poor image quality on reference images | Seeds marked on TPS by planner then marked with cross on DRR by treatment staff. | 1 |
| | Seed position inconsistent | Marker migration | Training regarding risk of migration and effect of rotations | 2 |
| **Action** | Potential for geographic miss | Lack of understanding of protocols | Training regarding protocol action levels | 2 |
| | Potential for geographic miss | Individual patient anatomy anomalies | Training with specific case examples | 2 |

A**ppendix VII**

**IGRT Training programme**

The IGRT training programme should cover 3 aspects

- Acquisition process – this could be covered in a formal presentation either delivered face to face or electronically. This should be accompanied by appropriate written documents which could be followed when practising using a phantom. Issues relating to imaging dose and quality should also be included
- Analysis process – cover in presentation and written instructions. A database of patient images for all IGRT techniques and anatomical sites should be available for practice
- Action - guidance for the timing and frequency of actions with explanation of the site specific protocols

**Assessment**

Assessment can be a combination of self assessment and peer assessment. For example workbooks could be used to explain each IGRT technology system and the applications with self assessment of baseline skills and further reading to develop greater understanding. The workbooks, ideally to be developed by the core site specialist multi-professional group, could be general e.g. use of kV CBCT or site specific for complex cases e.g. adaptive bladder, stereotactic lung. Competency assessments using a database of images to match against a standard can then also be used with a predetermined threshold for acceptable clinical competence.

Suggested contents of a workbook:

- Departmental work instructions
- Relevant journal articles for use of the technique for that anatomical site
- CT Anatomy (and test).

The use of VERT should be considered and utilised as appropriate. Otherwise a treatment planning system may be used where the GTV, OAR would be pre-outlined for reference. The trainee could contour the structures with the reference contours turned off and then compare.

- Detail of staging, epidemiology/aetiology, current management and treatment options
- Relevant clinical trials for this anatomical site
- Assessment of competency which could include:-

    (i) Self assessment of baseline skills with questions to verify learning

    (ii) Record of image analysis registrations

    (iii) Specific learning objectives

    (iv) Portfolio of relevant experience

    (v) Evidence of observation of registration/action

A competency assessment program should not only assess image analysis skills but also the decision making process for appropriate action. This may require additional training for example DVH interpretation, IMRT/VMAT implications for image guidance as well as individual cases where anatomy anomalies may affect the action.

Regular updates should be mandated, the frequency of which will depend on departmental rotation time, the number of IGRT capable linacs and sites treated on each linacs. Ideally annual updates are recommended together with re-assessment of competence after a period away form the specific technology.