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Radiation Hygiene Requirements for IGRT (Image Guided Radiotherapy)

Recommendation by the German Commission on Radiological Protection

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**Strahlenhygienische Anforderungen an IGRT (image guided
radiotherapy/bildgeführte Strahlentherapie)**

Empfehlung der Strahlenschutzkommission mit wissenschaftlicher Begründung

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Contents

Recommendation	4
Scientific Reasoning	6
1 Introduction	6
2 Definitions and Issues	7
3 Analysis of Positioning Errors in Radiation Therapy	11
4 Dose Deposition from Imaging Procedures	12
4.1 Planar imaging (MV and kV)	12
4.2 Cone Beam CT (CBCT)	13
4.2.1 kV image acquisition	13
4.2.2 MV imaging	14
4.3 Helical CT	14
4.3.1 kV imaging	14
4.3.2 MV imaging	14
5 Dose Distribution in Imaging (in Relation to Dose Distribution in Radiotherapy)	15
6 Implications for Technical Development	15
7 Relevance of Dose Depositions from IGRT in Relation to the Dose from Radiotherapy	16
8 Imaging Frequency Depending on the Irradiation Technique/Indication	17
Abbreviations	18
References	19

Recommendation

For decades, the positioning of the patient for radiotherapy consisted of alignment of skin marks with fixed lasers in the treatment room. The skin marks were placed during a single imaging session, e.g. a treatment planning CT session, before the patient began a course of radiotherapy. However, this system did not allow for control – which may be required on a daily basis – of the position of internal organs (organ tracking). In recent years, image guided radiotherapy (IGRT) has increasingly provided the opportunity to determine the position of the target volume and organs at risk immediately prior to an irradiation fraction. In general, this involves procedures which are based on the application of ionising radiation.

Planar imaging, for which an x-ray source producing energies in the kV or MV range is integrated into the moving part of the irradiation device (gantry), can be a reliable tool for quick and reliable imaging if the examination is focused exclusively on bony structures. Imaging with a standard x-ray tube (kV imaging) is preferable to the sole control of the isocentre with the treatment beam (MV imaging) because of better image quality and lower dose. In future, using the treatment beam for imaging should be limited to the purpose of monitoring the radiation field, which is required under radiation protection legislation.

Three-dimensional imaging can be realised directly at the accelerator on the basis of helical CT or cone beam CT (CBCT) with kV or MV photon radiation. These techniques provide a higher information yield (soft tissue contrast, 3D images), but they also require higher doses for all irradiated volumes as compared to planar kV imaging, and the volume at risk of stochastic radiation effects is expanded (stochastic risk volume, SRV). Particularly in those clinical situations where there is a risk of secondary tumour formation from high imaging doses (e.g. in children, young adults, and patients with good prognoses and relevant survival times), the potential benefits and risks of these procedures must be weighed against each other beforehand in a differentiated approach.

Even with optimal imaging, the quality of reproducible *patient positioning* must be given high priority, and must be ensured through appropriate positioning aids or procedures.

Daily imaging for patient positioning allows maximum precision to be achieved during treatment. Positioning protocols which do not include verification prior to each treatment fraction require lower doses but also offer reduced positioning certainty and accuracy, which means that compared with daily imaging protocols, extended safety margins (PTV) are needed to compensate for positioning errors. The potential benefit of daily positioning control with imaging techniques should therefore be weighed against the benefits of a protocol with a lower control frequency, taking into account the parameters relevant for secondary tumour formation, such as age of the patient, disease aggressiveness, organs at risk near the target volume etc. As a rule, in case of curative therapy protocols with high doses per fraction (e.g. stereotaxis), control for each fraction is preferable. Regardless of this, the frequency of imaging must always be based on the principles of justifying indication.

Among the available IGRT methods, preference should be given to methods which ensure sufficient image quality for positioning control while entailing the lowest dose deposition from imaging. Volume imaging is to be chosen if dose application is problematic due to a high total treatment dose required close to organs at risk.

Quality control standards, as laid down for diagnostic systems in the X-ray Ordinance, must be applied for all imaging systems used in the context of IGRT. In particular, technical processes must be established which document the imaging dose or allow the user to estimate the applied dose. These aspects must be considered by manufacturers when developing the

relevant technology. Manufacturers must be urged to advance technological developments with a view to reducing dose for imaging while maintaining appropriate image quality and develop systems for IGRT without using ionising radiation.

Moreover, suitable measures taken by manufacturers and additional quality controls must ensure that the isocentres of imaging and irradiation are identical in order to avoid new systematic uncertainties occurring in the treatment chain.

Scientific Reasoning

1 Introduction

Until now, verification of patient position has been performed with port films (PI) using the megavolt (MV) treatment beam (field control images, verification images), although films have recently been replaced with electronic portal imaging devices (EPIDs). Today, low energy photon sources (kV) and an additional EPID mounted to the accelerator gantry are available. These devices can be used in various applications for planar imaging, including tumour tracking (i.e. for monitoring tumour movements) or – with a rotating gantry – to generate volume image data sets (cone beam CT, CBCT). This type of CBCT (MV CBCT) can also be generated using the MV treatment beam. Other options available are conventional helical CT in the treatment room, with the imaging isocentre aligned to the irradiation isocentre, and – as a special application in a dedicated irradiation system for helical intensity-modulated radiotherapy – helical MV CT.

The various modalities differ in terms of their information yield and hence their positioning accuracy, as well as in the dose received by the patient in addition to the MV treatment dose, especially in tissues outside the target volume. Planar MV images that are limited to the treatment field do not cause any additional dose but are often difficult to interpret. Orthogonal MV images which are produced additionally to the treatment beams result in additional dose deposition outside the target area (typically ~ 30 mGy/image, mean energy dose in the imaging volume), but make verification of the isocentre easier. Both techniques primarily detect bony structures. Orthogonal kV images with devices designed specifically for this purpose produce images of better quality at a very low dose (< 1 mGy), with dependable imaging of bony structures; but poor imaging of soft tissue structures. Therefore the use of implanted markers in order to localise soft tissue structures indirectly is required. Helical kV CT in the treatment room produces volume image data sets of excellent quality, comparable to diagnostic imaging (bony structures and soft tissue). Dose deposition corresponds to that occurring in diagnostic radiology (10 - 15 mGy/scan). Helical MV CT is currently only established in a specially integrated therapy system (helical radiotherapy) and generates high-quality image data sets for bony structures and datasets of adequate quality for soft tissue structures with dose deposition of 10 - 20 mGy, but does not achieve the quality of helical kV CT and kV CBCT. MV and kV CBCT provide outstanding volume image data sets with excellent imaging of bony structures, comparable with that achieved with diagnostic techniques, and adequate imaging of soft tissue structures. While kV CBCT results in a dose deposition of approx. 10 - 30 mGy, MV CBCT requires higher nominal doses (minimum 80 - 100 mGy) than the other modalities without achieving the same image quality.

Daily volume imaging causes a dose deposition whose effect – in terms of the additional risk of secondary tumour formation – must be estimated, whereas the risk posed by planar KV imaging is negligible. A 0.5 - 1% increase in secondary cancer risk (Kan et al., 2008; Trott 2009) can serve as the upper estimate for volume imaging, depending on the acquisition parameters. This must be viewed in relation to a secondary tumour risk of approximately 1% after conventional radiotherapy and $\sim 1.5\%$ after intensity-modulated radiation therapy (IMRT) with 6 MV. The increased secondary tumour risk associated with IMRT is steadily decreasing at present due to increased efficiency of planning systems with regard to the primary dose (monitor units, MU). A reduction in the required dose, and hence the reduced risk from imaging, is made possible through the use of more sensitive detectors.

The dramatically reduced effectiveness of radiotherapy resulting from systematic positioning (setup) errors has been demonstrated in major studies. Daily imaging offers potential benefits for the patient by providing greater positioning certainty and, in some cases, the option of reducing safety margins, hence decreasing normal tissue exposure. Potential disadvantages are, first and foremost, the secondary cancer risk and, in a few exceptional cases (highly radiation-sensitive tissues and organs) the induction of deterministic effects. However, it must be assumed that the benefits outweigh the possible disadvantages. Weighing up these factors, an optimal imaging protocol should be selected for each patient / each clinical paradigm on an individual basis.

Stereotactic ultrasound or implantable radiofrequency (RF) transponders offer an alternative to the use of ionising radiation, provided that the target area is accessible for these techniques. The scope to use them should be regularly reviewed when justifying the choice of methods.

2 Definitions and Issues

To achieve optimal tumour control with acceptable side effects, curative radiotherapy requires the application of a sufficient dose in the target volume, while dose to surrounding tissues (organs at risk) is minimised. This is achieved through increasing alignment (conformation) of the high dose volume to the planning target volume (PTV). The prerequisite for this is stable positioning of the patient relative to the irradiation unit. Difficulties arise particularly with the treatment of extracranial targets, which are especially susceptible to positioning errors and organ movements (typically due to respiration or changing organ volumes due to organ filling).

Although the application of complex dose distributions is now possible, in principle, for all targets with modern irradiation techniques such as intensity-modulated radiation therapy (IMRT), precise patient positioning has been difficult to achieve, or has been achievable only with great effort (immobilisation of the patient), and therefore requires appropriate monitoring.

The various volumes (clinical target volume, planning target volume, treatment volume – see Figure 1) are defined in ICRU 62 (ICRU 1999).

To compensate for random and systematic positioning errors, such as those caused by movement of the tumour (gross tumour volume, GTV), a safety margin is typically added to the clinical target volume (CTV). The resulting volume is known as the planning target volume (PTV). Furthermore, physical conditions may mean that the treatment volume (TV) which is exposed to the curative dose cannot be limited solely to the planning target volume (PTV). As a consequence, parts of organs at risk may be inside the PTV or TV, whose tolerance dose then limits the target volume dose (Schaly et al., 2005; Song et al., 2005). If the correct position of the target volume and organs at risk are known immediately prior to treatment and if the patient's position is then corrected according to the displacement of the target volume, it is possible to reduce the safety margin around the CTV and thus lower the dose in the PTV and also in organs at risk (Little et al., 2003).

GTV: Gross Tumour Volume: the demonstrated tumour

CTV: Clinical Target Volume: GTV plus volumes with suspected (subclinical) tumour, e.g. a safety margin around the GTV

PTV: Planning Target Volume: CTV plus a margin to account for variations in size, shape, and position relative to the treatment beam as well as technical inaccuracies

TV: Treatment Volume: the volume which receives a dose that is considered significant for local cure or palliation

IV: Irradiated Volume (IV): the tissue volume that is considered significant in relation to normal tissue tolerance

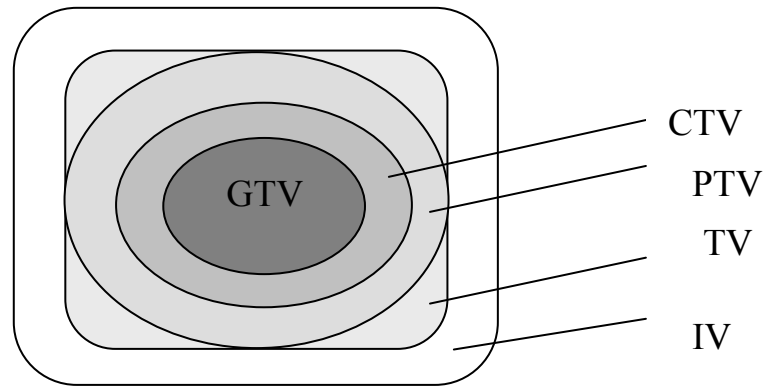


Figure 1: Schematic illustration of the different target volumes as defined by the ICRU

Within the ICRU treatment volume effects in normal tissue must be anticipated. Besides this treatment volume, other “biological” volumes must be defined for the purpose of the present analysis. They include the *stochastic risk volume (SRV)*, defined as the volume in which stochastic effects (e.g. tumour induction) may be anticipated. It is also important to take into account those volumes which are exposed to a dose exceeding the tissue- or organ-specific radiation tolerance of the normal tissue within that volume but without clinical effects necessarily occurring; these include the “organs at risk” (OAR), according to the ICRU. These volumes are termed *deterministic risk volumes (DRV)* below.

The dose limits of the DRV are thus dependent on the tolerance (for deterministic effects) of the organs and tissues located in this volume. For example, for the lens of the eye (cataractogenesis), a lower limit of 0.8 Gy can be assumed (SSK 2009; Ainsbury et al., 2009); for the testis (impaired spermatogenesis), it is 0.1 Gy; for the ovaries (permanent sterility), 2.5 Gy; for bone marrow (clinically significant impairment of blood formation), 0.5 Gy; for intestinal mucosa, 5 - 12 Gy; for the skin and the oral mucosa (ulceration), 10 - 20 Gy, etc. (SSK 2008). The irradiated volume (IV), according to the ICRU, thus includes both the DRV and the SRV. DRV und SRV may partially overlap (see Figures 2 and 3), depending on the tissues and organs located there and their sensitivity to deterministic and stochastic effects.

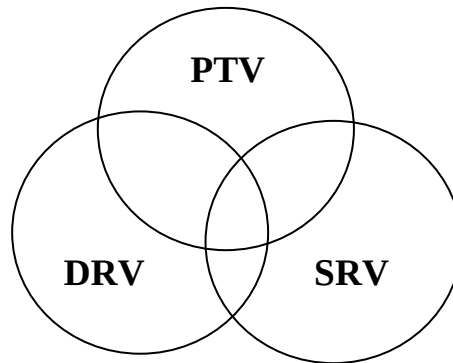


Figure 2: Biologically determined volumes in radiotherapy

Besides the PTV, as defined by the ICRU, when planning and delivering radiotherapy, including imaging, it is essential to take into account volumes in which there is a risk of deterministic radiation effects (deterministic risk volume, DRV); these volumes are determined by the radiation tolerance of the tissues/organs located within the irradiated volume and their position relative to the PTV. In addition, volumes must also be considered in which stochastic radiation effects may occur (stochastic risk volume, SRV). Here too, the definition depends on tissue / organ type and its sensitivity to stochastic effects.

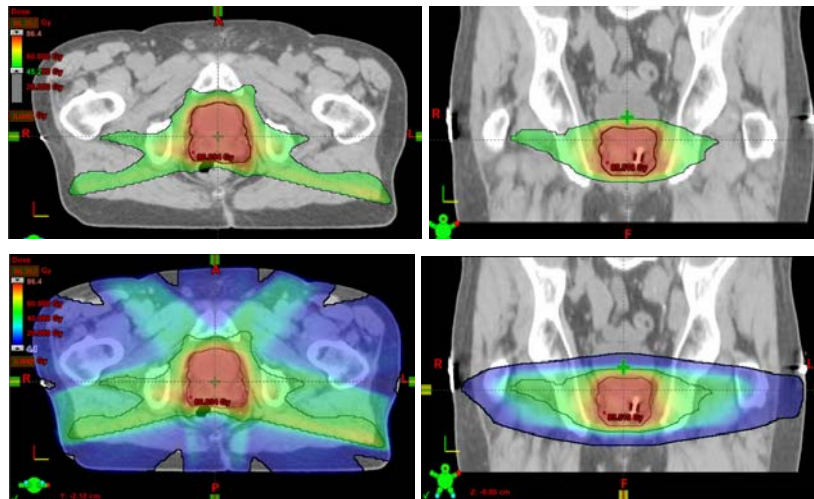


Figure 3: An example of treatment planning for prostate cancer: extent of the target volume and the volumes exposed to > 45 Gy and > 4 Gy

The figures show the dose distribution for irradiation of a prostate cancer at two levels. The high dose volume (PTV) is marked in red on all the images. The images at the top show the volumes (green) exposed to > 45 Gy. These correspond to the DRV in the relevant organs at risk (bladder, rectum, bony structures in the pelvic girdle and parts of the proximal femur). The images at the bottom depict volumes (blue) which are exposed to > 4 Gy (approx. 5% isodose) and represent the SRV. They also include, in this situation, the bladder wall and the rectum (due to secondary and primary tumour induction), but also – according to the risk estimates – the bone marrow in the pelvic bones. In addition, during radiotherapy of prostate cancer, according to Brenner et al. (Brenner et al., 2000), the lung must also be included in the SRV. However, this is usually not included in standard treatment planning.

For decades, the positioning of the patient for radiotherapy consisted of alignment of skin marks with fixed lasers in the treatment room. The skin marks were placed during a single imaging session, e.g. a treatment planning CT session, before the patient began a course of radiotherapy. However, this system did not allow for control – which may be required on a daily basis – of the position of the planning target volume (PTV) and critical internal organs. In recent years, “image guidance”, or “image guided radiotherapy (IGRT)” has increasingly provided the opportunity to determine the position of the target volume (or suitable surrogate markers) and organs at risk immediately prior to an irradiation fraction using imaging techniques, typically in the treatment room. In general, this involves procedures which are based on the application of ionising radiation. The American Society for Radiation Oncology (ASTRO) recently published Practice Guidelines which contain general methodological recommendations for IGRT procedures (Potters et al., 2010). The radiation hygiene aspects of this procedure will be assessed here as the basis for a relevant recommendation. For IGRT – in contrast to curative dose distribution in conformal therapy (SSK 2010) – it is the SRV which is primarily relevant.

The standard procedure for IGRT to determine the position of the patient has been to acquire orthogonal field controls (portal images, PI) of the patient with the treatment beam using an open field and a low dose, expressed in a low number of monitor units (MU) (Hurkmans et al., 2001). These images, which are generated with X-ray film or an *electronic portal imaging device* (EPID), provide information about the positioning of the patient’s bony structure. If the bone itself is not the target organ, bony structures can be used as a surrogate for the actual position of the soft tissue. After matching the PI to reference images produced earlier, positioning deviation can be calculated (2D/2D matching). Portal imaging with the treatment beam (with modern linear accelerators with radiation energy in the megavolt (MV) range, using *films*) was the standard procedure for patient positioning in recent decades. Due to the predominating Compton Effect, however, image quality was relatively poor. When images were acquired from angles analogous to the treatment beam orientations, the dose from the PI was taken into account in the monitor units. Dose deposition additional to the curative dose always results when images were acquired from angles different from the treatment beam orientations. Furthermore, this dose is deposited in sites which are not reached directly by the treatment beam. This dose, which is additional to the planned curative dose, depends on the mode of image acquisition. Electronic portal imaging based on amorphous silicon detectors has significantly improved image quality for MV imaging, but still suffers from the same problems as film-based MV imaging: lack of soft tissue contrast and confinement to 2D/2D or 2D/3D image matching (matching of 2D control images with a 3D data set of angle-dependent digitally-reconstructed radiographs (DRR)).

In some situations, immediate positional verification can be successfully performed in the hospital using ultrasound. Stereotactic procedures are also available for this purpose (Morr et al., 2002; Trichter and Ennis, 2003).

Higher-quality imaging of bony structures can be achieved with the use of lower-energy photons, e.g. with an X-ray source installed in the treatment room which supplies photon energy of 80-140 keV. However, here too, the soft tissue information is generally poor and is still limited to high contrast situations such as identification of lung tumours (Fuss et al., 2007; Wurm et al., 2006).

If, however, the X-ray source and detector are mounted on the rotating part of the linear accelerator (gantry), it is not only possible to acquire planar images, but also to acquire a series of projections of the patient during a 360° rotation and thus perform a “cone-beam CT scan” (CBCT). These can be used for a volume reconstruction in transversal, coronal and

sagittal slices providing 3D bone and soft tissue image information (Jaffray et al., 2002; Letourneau et al., 2005; McBain et al., 2006). With these reconstructions, it is possible to locate the target volume immediately before a treatment session and to position the patient correctly based on matching of CBCT and treatment planning CT. A comparable approach to 3D imaging was also performed using the MV treatment beam together with a suitable detector, albeit with the limitations in image quality described above (Pouliot et al., 2005). Furthermore, dedicated helical CT systems in the treatment room, with a fixed relationship between its imaging isocentre and the radiation isocentre of the linear accelerator, have been developed (Fung et al., 2003; Stutzel et al., 2008).

Recently, helical radiotherapy systems have been developed in which the patient is moved lengthwise through a treatment beam while the radiation head itself rotates around the patient. In these systems, helical beam guidance can be used both for imaging (MV) and for treatment (Stutzel et al., 2008).

In order to maximise the benefits of image guidance, described above, in terms of limiting exposure of organs at risk, either the target position can be visualised and, if necessary, corrected immediately before each treatment fraction (online procedure) (Li et al., 2006; Wu et al., 2006), or the treatment margin can be adapted to the estimated target movement during the course of the treatment sessions (offline procedure) (Yan et al., 2000).

Image guidance with photons results in additional dose to the patient. Determining this dose and evaluating its possible effects are therefore of great interest.

The present analysis will therefore initially consider the potential benefits of image guided radiotherapy. The “state of the art” in imaging technology at the accelerator will then be described, and the doses deposited in this context and the dose distribution characteristics will be discussed, both numerically and in terms of their biological effects in relation to dose deposition from radiotherapy.

The development of alternative procedures without the use of ionising radiation, such as stereotactic ultrasound or implantable radiofrequency (TF) transponders, should be progressed. Where available, these procedures may be used as the preferred option in a few specific clinical situations.

3 Analysis of Positioning Errors in Radiation Therapy

There are two main types of positioning error which adversely affect accuracy in radiotherapy. First, various factors – such as inaccuracy of skin markings, variations in organ filling during the acquisition of image data for treatment planning, etc. – may result in *systematic* positioning (setup) errors becoming established in the treatment planning and application chain. *Random* errors can occur as a result of variations in daily positioning, typically due to respiration, anatomical changes caused by tumour shrinkage, or unavoidable changes in patient setup.

Systematic errors in particular, but also random errors can have a dramatic effect on clinical outcomes. These will be discussed below, with particular reference to prostate cancer and head-and-neck tumours.

In two major randomised studies on prostate-cancer radiotherapy, it was demonstrated that incorrect positioning during radiotherapy significantly decreases tumour control rates (Chow et al., 2008; Heemsbergen et al., 2007). Although the systematic setup errors investigated in these studies is not quantified in the publications, they probably fell within the 1 - 3 cm range. This resulted in a decrease of approximately 30% in tumour control (expressed in the

biochemical control, i.e. a permanent decrease in PSA level). This much poorer outcome of radiotherapy means that in a worst-case scenario, the dose reaching some parts of the tumour was reduced by 16 - 18 Gy and must have been deposited instead in adjacent healthy tissue (Chow et al., 2008). The volume of organs at risk (DRV) exposed to curative dose is in many cases associated with the rate of induced deterministic side-effects.

In the head-and-neck, a reduction in positioning error from 3 - 5 mm to 1 mm can reduce the exposed volume of the parotid gland (DRV) if the target volume is directly adjacent to this gland. In these cases, it is possible to reduce the probability of impairment of parotid gland function by 10 - 15% (Delana et al., 2009).

4 Dose Deposition from Imaging Procedures

4.1 Planar imaging (MV and kV)

Dose deposition from imaging will be discussed with reference to prostate-cancer radiotherapy. For two orthogonal MV images with the treatment beam and the standard dose (generally 5 monitor units per image for film-based PI), the additional rectal dose amounts to approximately 66 mGy (Walter et al., 2007). The corresponding skin doses are approximately 100 - 130 mGy. In prostate treatment up to a total dose of 60 Gy (delivered in individual doses of 2 Gy) and twice-weekly positional verification, the rectal dose from imaging amounts to 790 mGy; with daily verification, it increases to almost 2 Gy. Moreover this dose is distributed across the entire pelvis minor and is not limited to the target volume only. These doses can in some circumstances be reduced by using a lower number of monitor units.

The additional physical dose deposited, e.g. in the rectum, as a result of MV PI can, in principle, be taken into account during treatment planning in the doses to the organs at risk. This procedure is already applied in some departments (Ganswindt et al., 2005; Vetterli et al., 2006), and should be the standard aspired to by all departments in future.

The dose to the rectum for two portal images made with the kV source was 99% lower – amounting to 1% – than the dose for MV images described above; the skin dose was 2%. Absolute doses between 0.1 mGy in the centre of the pelvis (anterior-posterior (AP) image) and 1 mGy at the surface (lateral PI) and rectal doses of 0.1 mGy from pelvic imaging are described (Walter et al., 2007).

The CyberKnife system is a special case in planar kV imaging. The CyberKnife incorporates a linear accelerator mounted on a free-moving general purpose industrial robotic arm. This system tracks targets that move. It uses the surrogate marker technique (with markers fixed to the thorax) and localises the tumour trajectory; this is carried out after matching of planar imaging and acquisition of the surrogate marker position to produce an individual patient movement model. During treatment, this model is then verified at close intervals using planar kV imaging. According to the literature, the cumulative patient surface entrance dose was estimated to be equal to 0.7 mGy per acquisition during a CyberKnife treatment session; an average of 50 images per treatment session results in a cumulative dose of 3.5 mGy and thus, depending on the number of fractions (typically 3 – 5), a total dose of approximately 10 - 20 mGy (Antypas and Pantelis, 2008, and Accuray, pers. comm.).

4.2 Cone Beam CT (CBCT)

4.2.1 kV image acquisition

The anticipated tolerable maximum and minimum doses ($D_{\max}$ und $D_{\min}$), e.g. in the rectum, can be calculated for a CBCT acquisition from the results of dose measurements of anterior-posterior (AP) and lateral images as follows:

$$D_{\max} = n/5 D_{\text{ap}} \text{ and } D_{\min} = n/5 D_{\text{lat}},$$

where D_{ap} is the dose for an AP image with 5 acquired individual frames, D_{lat} is the dose for a lateral image (also based on 5 frames) and n is the number of frames for one CT scan.

Exemplary experimental investigations confirm the validity of this formula. For example, the average dose inside the rectum for a 360 ° volume scan was 17.2 ± 2.8 mGy (Walter et al., 2007), which is inside the expected range from $D_{\min} = 16.9$ mGy to $D_{\max} = 24.7$ mGy. This is approximately 73% lower than for two MV portal images at 5 MU/exposure and is in the range of what is reported with anthropomorphic phantom measurements (Amer et al., 2007; Wen et al., 2007). However, the CTDI-phantom measurements show that the dose 1 cm below the surface is higher than the dose measured in the middle of the phantom (due to the energy of the photons in the kV range and the corresponding depth dose distribution). The peripheral dose at 1 cm depth in the phantom corresponds to approximately 90% of the skin dose for 120 kV photon¹ depth-dose-curve. Hence a conservative estimation of the skin dose would be 28 mGy (DGMP 2000). This corresponds with other reported CTDI-phantom measurements (Wen et al., 2002), the exact values depending on the acquisition protocol (full vs. partial rotation, field of view (FOV), etc.).

These exemplary estimations and measurements match the data available in the literature. Standard clinical imaging currently results in a central dose of < 30 mGy, whereby 60 mGy is the upper limit value referred to in publications (Islam et al., 2006; Kan et al., 2008; Perks et al., 2008; Stutzel et al., 2008). Depending on the imaging protocol and patient characteristics, the peripheral dose/skin dose may be slightly lower than or equal to this dose. Typically, however, it is up to 40% higher than the central dose (Islam et al., 2006; Kan et al., 2008; Perks et al., 2008; Walter et al., 2007).

If the dose on the central ray of the cone beam is 30 mGy, the dose in the centre of the body in a longitudinal distance (i.e. vertically to the rotation level) of 7 respectively 12 cm to the edge of the primary beam and therefore -with a total field of view of 26 cm- of 20 respectively 25 cm from the central ray is 5 mGy and 2 mGy (Perks et al., 2008) averaged over various phantom diameters (patient diameters). Patient diameter is in this case of minor influence on the dose outside the primary beam.

With a fraction dose of 2 Gy, the scattered radiation dose with an IMRT is 10 mGy and 4 mGy measured 0 and 25 cm respectively from the central axis of the patient (with no correction for radiation quality) (Perks et al., 2008). Thus the dose from kV CBCT-based IGRT is approximately half the amount of the scattered radiation dose associated with a IMRT (Perks et al., 2008; Stern 1999) at a distant point outside the field.

In a medium term, optimisation of imaging protocols can be expected to result in further dose reduction in kV CBCT. Doses in high contrast situations, such as lung imaging (mediastinum) can already be lowered to 6 mGy by protocol optimisation (Amer et al., 2002).

¹ Here, “120 kV photons” denotes the X-ray spectrum produced by a tube voltage of 120 kV.

Even lower doses are possible when image reconstruction is based on fewer projections and reduced acquisition angle (Islam et al., 2006; Sykes et al., 2005; Yin et al., 2005) and if quantum efficiency and signal-to-noise ratio of detectors are further improved (Sillanpaa et al., 2006). This can be anticipated in the near future, as the clinical introduction of the next generation of detectors is imminent.

4.2.2 MV imaging

Doses required for MV CBCT are, by virtue of the underlying principles, currently higher than the values reported for kV CBCT. Initially, the literature reported doses of 50–150 mGy to yield images of sufficient quality with experimental devices for MV-based volume imaging (Gayou et al., 2007; Morin et al., 2007; Sillanpaa et al., 2006). For imaging in the head-and-neck, 50 - 70 mGy and in the pelvis 80 - 100 mGy currently appear to be realistic estimations of the minimum dose required to produce images of acceptable quality. This dose is therefore higher than for other modalities such as kV CBCT, helical MV CT or helical kV CT, although it must be kept in mind that the relevant imaging parameters (signal-to-noise ratio, contrast-to-noise ratio, spatial resolution, etc.) are poorer throughout (Stutzel et al., 2008). Even for high doses in the 170 mGy range, the signal-to-noise ratio for MV CBCT was less than 20% compared with a kV CBCT prototype installed on the same linear accelerator with dose deposition of only 15 - 30 mGy.

4.3 Helical CT

4.3.1 kV imaging

Dose deposition and image quality for helical kV computed tomography (CT) in the accelerator room are well-documented, as this usually combines a regular diagnostic helical CT as a freestanding unit combined with a regular linear accelerator. Accurate patient positioning is generally guaranteed by establishing a defined spatial relationship between the CT and the accelerator isocentres. The positioning process is slightly more complicated than with solutions carried out directly at the accelerator, with a higher risk of patient movement between imaging and treatment, as this procedure involves the translation of the treatment couch over some distance and/or a rotation. Although this technique requires more space and therefore cannot be realised in many treatment rooms, it should be considered when building new facilities. It delivers by far the best image quality with outstanding soft tissue contrast at very low doses (10 - 15 mGy) per acquisition. These can be further substantially reduced in certain clinical situations when poorer image quality is acceptable.

4.3.2 MV imaging

Recently, helical irradiation procedures have been developed in which the radiation source is moved in a spiral shape around the patient (“tomotherapy”). Preliminary published data on the applied doses during MV imaging using helical techniques are higher (30 mGy) than measurements for CBCT (Forrest et al., 2004).

The signal-to-noise ratio is constant for doses between 10 and 30 mGy. These lie within the range that can be achieved with low dose kV CBCT (10 mGy) (Shah et al., 2008; Stutzel et al., 2008). Image quality for the imaging dose now established as standard for this technique (15 - 20 mGy) is acceptable

5 Dose Distribution in Imaging (in Relation to Dose Distribution in Radiotherapy)

The characteristics of dose distribution in imaging, in relation to dose distribution in radiotherapy, were partly addressed in the previous chapter in the discussion of dose deposition in the individual imaging modalities. In this context, lateral dose distribution in the target volume area must be distinguished from the characteristics of dose deposition along the longitudinal axis with increasing distance from the primary beam.

With regard to *lateral dose distribution*, the general principle which applies in therapeutic applications using modern techniques (photon energy ≥ 4 MV and at least 3 beam directions) is that the maximum dose is applied in the target volume (PTV) along the beam direction, while peripherally, the dose decreases. Dose distributions with dose peaks outside the target volume, which occur e.g. in single-field therapies and opposed field irradiation with low energy, are generally only accepted in palliative situations.

In contrast to the distribution of the curative dose, the methods used for image guidance – depending on the imaging protocol (partial vs. full-circle rotation) – generally produce even (MV CBCT with full-circle rotation, helical MV-CT), non-rotation-symmetrical (planar kV and MV imaging, MV and kV CBCT with partial rotation) or trough-shaped dose distributions with peripheral maximums and central minimums (kV CBCT with full-circle rotation) (Morin et al., 2007).

As described above, depending on the imaging protocol, radiation energy used, and scan volume diameter, the peripheral dose/skin dose (in the DRV, SRV) may be slightly lower than, equal to – or, typically – up to 40% higher than the central dose (Islam et al., 2006; Kan et al., 2008; Perks et al., 2008; Walter et al., 2007). This is of particular relevance if highly radiation-sensitive structures (e.g. the lens of the eye, gonads) are located in proximity to the PTV, but it is also relevant in relation to radiation induction of tumours.

The *peripheral dose in the longitudinal direction of the body* decreases outside the scan volume, similar to the peripheral dose of therapeutic radiation (Perks et al., 2008; Stern, 1999), more steeply in the case of kV imaging due to better collimation.

6 Implications for Technical Development

From a radiation hygiene perspective, due to their physical properties, all techniques which perform imaging using the treatment beam are associated with higher doses of radiation, also outside the target volume/high dose volume, i.e. in the DRV and also in the SRV. Furthermore, the image quality achieved is limited, and in high-precision irradiation techniques in particular (e.g. stereotaxis), does not provide the required basis for assessment. For these reasons, preference must be given to the technical development of kV imaging systems.

Quality control standards, as laid down for diagnostic systems in the X-ray Ordinance, must be applied for all imaging systems used in the context of IGRT. In particular, technical processes must be established which document the imaging dose or allow the user to estimate the applied dose. These aspects must be considered by manufacturers when developing the relevant technology.

Moreover, suitable measures taken by manufacturers and additional quality controls must ensure that the isocentres of imaging and irradiation are identical in order to avoid new systematic errors occurring in the treatment chain.

7 Relevance of Dose Depositions from IGRT in Relation to the Dose from Radiotherapy

Radiotherapy can induce secondary tumours (Doerr and Herrmann, 2008; Tubiana, 2009). This risk is particularly significant in the case of children and young adults due to their life expectancy, but should also not be overlooked in the case of older patients who are undergoing curative radiotherapy and may have long survival times (e.g. irradiation of prostate or breast tumours) (Berrington et al., 2009; Brenner 2006). By definition, the IGRT-related dose in the SRV also contributes to radiation-induced tumour risk.

Complex irradiation techniques such as IMRT require verification of positioning to be performed at regular intervals. As a result, in addition to the already high dose deposition outside the target volume resulting from conformal techniques (SSK 2010), this results in additional radiation exposure in the patient's body, i.e. an expansion of the SRV/increased dose in the existing SRV. In the DRV, this additional dose is only relevant if it affects tissues which are very sensitive to radiation (e.g. the lens of the eye, gonads).

The IGRT dose *within the high dose volume* (HDV) is low compared with the curative dose. Nonetheless, it should not be overlooked, and must be properly documented. According to current knowledge, modification of the curative dose is not indicated.

The *peripheral dose* is the main focus of interest. Based on the above estimates, IGRT with CBCT increases the secondary tumour risk by < 2% compared with conventional radiotherapy without IGRT. There is a good match between these data and earlier publications (Kan et al., 2008) if the estimates are converted to the doses currently applied. Kan et al. estimate a secondary tumour risk of 2% to 4% for doses 2-3 times higher than those now applied in standard imaging protocols. This also produces a risk of < 2% for the present situation. Whereas the above estimates are similar for helical MV CT, helical kV CT and kV CBCT, they are somewhat higher for MV CBCT and lower for planar KV imaging.

By eliminating positioning (setup) errors, it may be possible to reduce the safety margin between CTV and PTV, resulting in a decrease in radiation fields and hence reducing the total amount of radiation energy deposited in the patient. This primarily benefits normal tissue in the SRV and DRV. For the irradiation of the prostate, a reduction of the safety margin by just 3 mm in a field size of 8 cm reduces total deposited energy by 15%. As soon as the use of IGRT allows significant reduction of the TV, the additional dose resulting from imaging is easily offset by a more targeted curative dose distribution overall.

The IGRT dose may also be relevant in relation to deterministic radiation damage (Perks et al., 2008). Even at low doses, azoospermia (temporary from 0.1 Gy, permanent from 2.5 - 3.5 Gy) (SSK 2008), loss of ovary function (from 2.0 – 2.5 Gy) (SSK 2008) or cataractogenesis (from < 0.8 Gy) (SSK 2009, Ainsbury et al., 2009) can occur. Furthermore, the high radiation sensitivity of the growing female breast in young girls during the prepubertal age is also of relevance in paediatric radiology (from 3 Gy) (Kolar et al., 1967).

Chow et al. (Chow et al., 2008) report on the effect of daily IGRT on dose distribution in organs at risk (in the DRV) in prostate-cancer radiotherapy (Brenner et al., 2000). Whereas the spatial dose distribution in the target volume and most organs at risk remained virtually unchanged by the IGRT dose, the head and neck of the femur received a much higher exposure due to kV radiation mainly being absorbed via photoelectric effects (high Z in bone). However, the cumulative dose from IGRT and IMRT was in the acceptable dose range for this structure. This was confirmed in a similar study by Ding et al. (Ding et al., 2008).

The lens of the eye is particularly sensitive to radiation. For IGRT (kV CBCT) during radiotherapy for head and neck tumours, doses of up to 60 - 80 mGy per acquisition were estimated, based on measurements and Monte Carlo simulations, albeit at settings which produced higher than standard doses (Kan et al., 2008). A more realistic estimate for current imaging protocols is 10 mGy per acquisition, producing a cumulative dose of 300 mGy for a standard fractionation with 30 fractions and daily CBCT. This dose could increase the risk of cataractogenesis (SSK 2009, Ainsbury et al., 2009).

8 Imaging Frequency Depending on the Irradiation Technique/Indication

IGRT can be used to reduce systematic error (Baum et al., 2005; Bel et al., 1996; Bortfeld et al., 2002) – which in many cases compensates for most of the positioning error – but can also be applied to reduce random error. Systematic error is defined as regular and identical deviation from the planned irradiation protocol (e.g. an incorrect table position). Random errors can occur irregularly and cause spontaneous deviations of varying magnitude (e.g. changes in organ position during the individual irradiation fractions).

Daily imaging initially enables the systematic error in the treatment chain to be identified and corrected. Thereafter, a review is carried out and, if necessary, the PTV modified in order to compensate for random error (Baum et al., 2005). However, this will not achieve permanent optimisation of the irradiation procedure, as further random errors, by their very nature, can occur. During the series of treatment sessions, further imaging is carried out less frequently in order to identify any potential change in the daily position of the PTV within the identified framework, or to determine whether this process must be repeated. If random treatment errors are also to be regularly reduced, daily imaging must be performed for direct positional correction.

Irradiation protocols with lower imaging frequency result in a low dose in all volumes. Nonetheless, with certain irradiation indications (e.g. prostate cancer), daily imaging has become routine in many departments with the requisite equipment. Perks et al. (Perks et al., 2008) cite two reasons for this: the reliability, performance and accuracy of the systems which enable imaging to be integrated into daily work processes. The high acceptance of this approach in clinical routine is based on the obvious logic that it allows the patient to be correctly positioned and irradiated during each fraction. This conflicts with proposals advocating less frequent imaging, during the course of radiotherapy, in order to identify and correct systematic errors (Perks et al., 2008).

At present, the decision on which of the two strategies to use depends on the clinical situation:

- If a moderate dose is sufficient to provide tumour control and the distance to dose-limiting organs at risk is such that random positioning errors will not result in a critical dose, a less frequent imaging protocol should be used to compensate for systematic error.
- If, on the other hand, dose-limiting tissue or organs are located in the immediate proximity of the target volume, daily imaging should be used.

As it is becoming apparent, for more and more clinical situations, that higher doses provide better tumour control rates, the latter method will be indicated more frequently in future. Nonetheless, here too, the frequency of imaging must always be based on the principles of justifying indication.

Abbreviations

ASTRO	American Society for Radiation Oncology
CBCT	Cone Beam CT
CTDI	Computed Tomography Dose Index
CTV	Clinical Target Volume
DRR	Digitally-Reconstructed Radiograph
DRV	Deterministic Risk Volume
EPID	Electronic Portal Imaging Device
GTV	Gross Tumour Volume
ICRU	International Commission on Radiation Units and Measurements
IGRT	Image Guided Radiotherapy
IMRT	Intensity-Modulated Radiation Therapy
IV	Irradiated Volume
MU	Monitor Units
OAR	Organs at Risk
PI	Portal Imaging
PSA	Prostate-Specific Antigen
PTV	Planning Target Volume
SRV	Stochastic Risk Volume
TV	Treatment Volume

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