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IMAGE GUIDED RADIATION THERAPY

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List of abbreviations

3D-CRT	3 dimensional conformal radiation therapy
BAT	B-mode Acquisition and Targeting
CBCT	Cone-beam Computed Tomography
CT	Computed Tomography
CTV	Clinical Target Volume
DRR	Digitally Reconstructed Radiograph
EPID	Electronic Portal Imaging Device
GTV	Gross Tumour Volume, the macroscopic tumor
ICRU	International Commission on Radiation Units and Measurements
IGRT	image guided radiation therapy
IMRT	intensity modulated radiation therapy
ITV	Internal Target Volume
MLC	multileaf-collimator
PTV	Planning Target Volume
SAD	source-axis distance
SSD	source-skin distance
VMAT	volumetric modulated arc therapy

1. Preface

Radiotherapy for cancer patients has a history of decades. Initially, orthovoltage and X-ray devices were used in teletherapy. Cobalt irradiation devices using the ^{60}Co isotope as radiation sources in radiotherapy treatment facilities in the early seventies and early nineties were a major step forward, making it possible to achieve the desired therapy. In the eighties and nineties, linear accelerators were purchased in many places that can artificially produce high-energy photon and electron beams without a radioactive source. Thanks to advances in computer technology, large numbers of irradiation planning software solutions became operational in the last decade of the last century, but especially after the turn of the millennium, opening the way for the routine three-dimensional, conformal radiation therapy design and implementation. After 2010 the use of so-called intensity modulated radiotherapy and volumetric modulated arc therapy widespread as well (IMRT, VMAT). The need for comparability of treatment results and the increasing complexity of the technology made it necessary to develop guiding protocols at international level. Increasingly accurate treatments required more accurate, standardized target volume determination, dose prescription, dose calculation and dose measurement. The rapid development of image-guided radiotherapy (IGRT) in recent years has made it possible to further improve accuracy. In this note, we summarize the theoretical background, the possibilities, and the tools for implementing this technique.

2. Irradiation techniques

2.1. 1D irradiation

One-dimensional irradiation planning in the current sense cannot be considered as a true planning procedure, but rather a dose calculation. This procedure is usually used for simple but quick radiotherapy (skin diseases, joint degenerative diseases, urgent palliative bone radiation, etc.).

As a first step, the treating physician will designate the dose point, which is located in the patient, most often in the geometric centre of the treatment area. Its position and depth from the skin surface (d , treatment depth) are determined by simple orthogonal X-rays or possibly by CT imaging. This is followed by the determination of the required field size (X and Y , length and width), which is also possible on the basis of the mentioned imaging tools. Finally, the required fraction dose (D) is defined.

Patient positioning can be isocentric or fixed source-surface distance (fixed SSD). This is also decided by the treating physician because the field size and treatment depth will be described as a function of the positioning method selected. In the isocentric setting, the isocentre of the irradiated image is at the point of dose specification, whereby the source surface distance is the difference between the source axis distance (SAD) and the dose prescription depth (d). SAD is a geometric feature of the machine, a given constant value, typically 100 cm for medical linear accelerators.

$$SSD = SAD - d$$

In a fixed SSD setting, the isocentre is placed at the entry point of the main beam to the skin surface. Consequently, the SSD is then the same as the SAD.

There is a possibility of so-called mixed mode setting, when positioning a patient according to a given SSD value, so that the isocentre may not be at the dose prescription point. These setup modes are shown below.

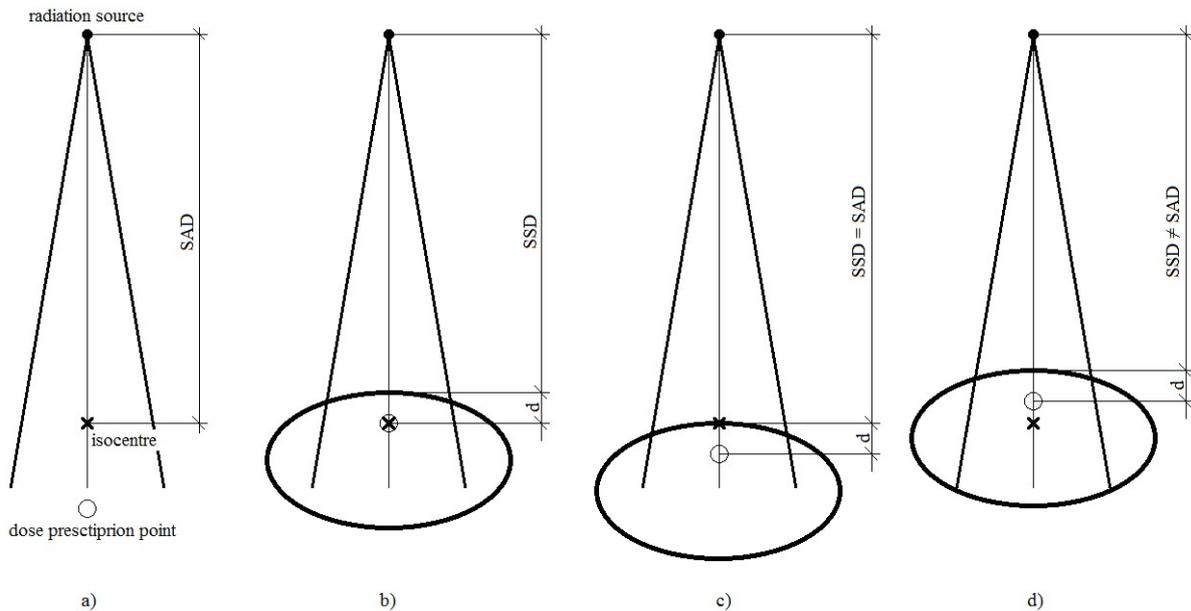


Figure 1.

- a) geometry of irradiation b) isocentric sep-up;
 c) fix SSD set-up; d) mixed mode set-up

Using the data above (SSD, d , X , Y , D) the required irradiation time can be calculated from the dataset model of the irradiating machine, taken during the so-called commissioning measurements.

The advantage of the method is that it requires a fast and small resource, as it does not necessarily require complicated imaging, contouring, irradiation planning, QA measurements. However, the disadvantage is that the delivered dose is known only at the dose prescription point. The dose to the surrounding tissues can only be estimated, and there is virtually no reliable information on the volume dose. Therefore, 1D dose calculation is used only where the irradiation area is well defined and the surrounding organs-at-risk and tissues are surely avoided.

2.2. 2D irradiation

2D radiation only has historical importance today and will not be discussed in detail. In essence, even with small computer capacities, it was possible to accurately calculate and display the dose distribution during irradiation on some axial CT slices. Typically, this method was widespread in the '90s, when computers were several orders of magnitude slower than today's devices. In the clinical routine, it would have been unacceptably long (up to days) to calculate the dose distribution on each axial slice of the patient, so the number of slices taken into consideration was limited to 3-5.

The advantage of the method is that it gives a much more accurate view of the dose distribution in the irradiated volume, although the total relative doses of each organ could still only be estimated.

A further disadvantage was the need to manual digitalization of CT slices from film according to the era, as well as the need for contouring and computing, which required significant additional resources and time.

With the advancement of computing technology and the rapid increase in computing speed, the 2D planning method has disappeared from the clinical routine and has been replaced by 3D radiation planning.

2.3. 3D irradiation

3D irradiation technology and irradiation design is always a multi-step, complex, resource-intensive and time-consuming process. Depending on the irradiated volume, CT scans or other imaging modalities should be performed to map the patient's anatomy. Images are captured and stored digitally in a computer database. The target volume and the organ-at-risk must be defined during the contouring process. The delivery of the prescribed dose to the target volume with the expected homogeneity, with maximum protection of the risk organs, can be achieved by a complex computational algorithm on a spatial computer model of all available axial slices, including particle transport. A major advantage of total spatial dose calculation is that the dose delivered to each image voxel is known, so that an accurate dose value is available at each point in the organs-at-risk and in the target volume, from which summary and statistical volume distribution can be calculated and analyzed.

The oldest, but still clinically valid type of 3D irradiation is the conformal method. The direction, weight, size, shape, and possible beam modifiers of the radiation fields used in the irradiation are set by the planning physicist on the basis of the patient's spatial digital reconstruction. This is followed by a dose calculation, then an evaluation of the dosimetric characteristics of the plan and, if necessary, modification or refinement of the plan. This is the so-called forward planning process.

The most modern and most complex irradiation technique is Intensity Modulated Radiation Therapy (IMRT). Planning is done by the "inverse" method: the defined dose criteria are loaded into an optimization module, then the planning system uses the optimization algorithm to generate the required fields and the modulation scheme of the beam intensity of each field. This is followed by dose calculation and evaluation. If modifications are required, the input

parameters might be changed. Due to their complexity, fields or modulation schemes should not be changed manually, and in some cases it is even not possible.

In the historical development of technology, one of these techniques was the emergence of stationary IMRT techniques. The beam modulating multileaf collimator (MLC) is located in the head of the irradiation machine. The MLC is an electronically movable collimator system consisting of radiation-absorbing leafs.



Figure 2: multi-leaf collimator¹

Intensity modulation can be created by a static (step-and-shoot) or a dynamic (sliding window) procedure (respective to their chronological appearance). In the former case, smaller subfields are directed to each part of the field, from which an additional dose can be delivered. During the MLC re-alignment between the individual subfields, the radiation beam is interrupted, so the irradiation occurs step-by-step. Thus, the dose is delivered at different intensities in each part of the field. In the second case, the leafs of the MLC are in constant motion during the course of the beam. The width, the opening and closing velocity of the current thin window left open by the opposing leaf pairs can be influenced by varying the velocity of the leafs. The field consists of sliding window next to each other.

The most up-to-date and widespread method of intensity modulated radiation therapy is rotational intensity modulation, also known as volume modulated arc therapy (VMAT). Although a separate name, logically all VMAT treatments are actually IMRT treatments. For historical reasons, however, IMRT refers to stationary field techniques, and VMAT (IMAT, RapidArc) to rotational field techniques. During VMAT treatment, the irradiation machine rotates continuously around the patient, with continuous radiation and complex, pre-planned MLC movement. The angular speed of rotation and the dose rate of the beam are not constant during delivery, but varies in the manner specified by the planning system.

2.4. Classification of irradiation techniques

The diagram below shows the relationship and classification of the above-mentioned irradiation techniques.

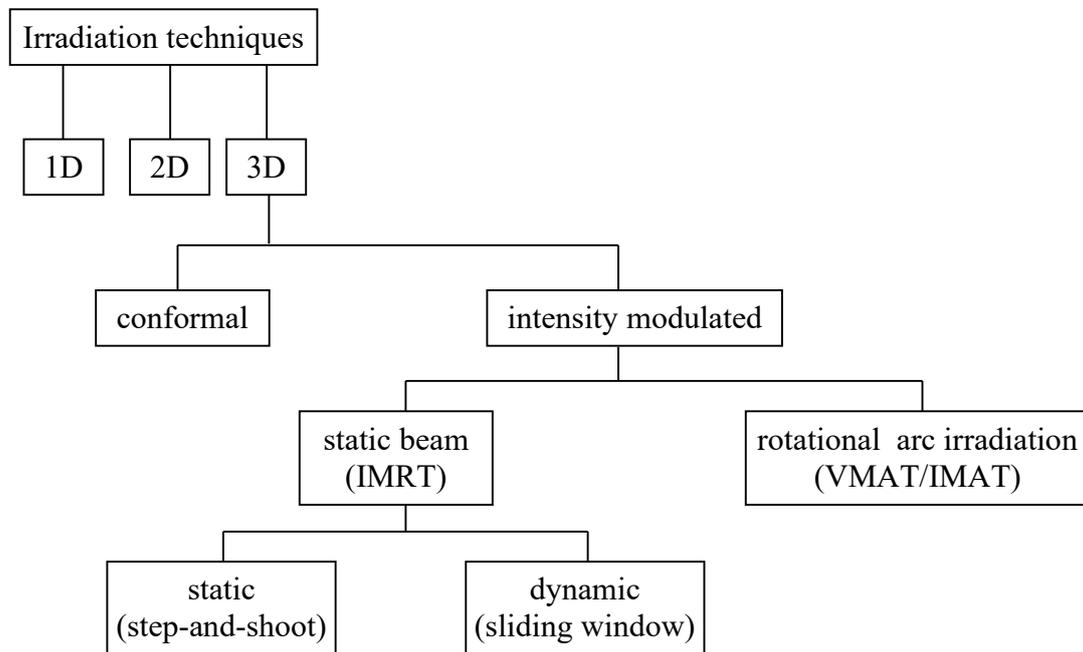


Figure 3: classification of irradiation techniques

As sophisticated irradiation techniques have evolved and became part of the daily clinical routine in recent decades, the accuracy of patient positioning has become increasingly important. While in the '60s and '70s the centimeter accuracy setting was satisfactory, nowadays 2-3 mm accuracy is already a general requirement, in some cases even the need for submillimeter positioning appears. This challenge led to the emergence of image guided radiotherapy techniques and the necessity of developing appropriate imaging technologies.

3. Determination of target volume

An important step in advanced 3D-CRT, IMRT, or VMAT radiation therapy for cancer patients is the accurate determination of the shape and extent of the target volume. The ICRU 50 and 62 international protocols record the nomenclature of the target volume.²

The use of sectional imaging procedures is essential for the designation of organs and areas to be protected, and for dose calculation during radiation planning. This mainly involves CT and MRI, less frequently PET-CT, SPECT-CT imaging. CT imaging is also essential for performing the dose calculation. This is because CT imaging and therapeutic irradiation have the same physical interaction (Compton scattering), so CT imaging contains the electron density map of the tissues that can be used to calculate the distribution of energy absorbed from radiation, ie. the dose distribution. The images are processed by computer contouring and irradiation design programs. On each slice, the organs-at-risk and the target area must be drawn. In this way, a unique three-dimensional computer reconstruction of the patient can be made.

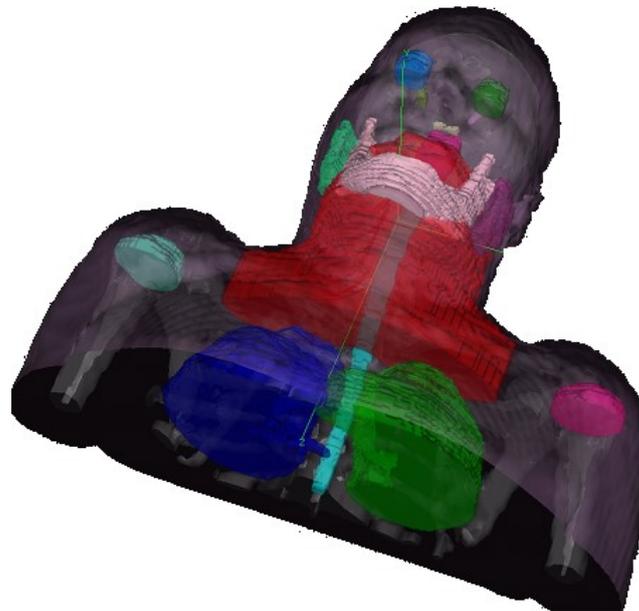


Figure 4: 3D reconstruction³

The target volume is determined in several steps. First, the macroscopic tumor on each axial view should be drawn, this is the GTV. Depending on the histological type and nature of the tumor, GTV should be extended taking into account known environmental microscopic infiltration not seen in the images, and the locoregional lymph nodes involved. The volume

thus determined is called CTV, which includes all areas to be covered by the therapeutic dose. However, the CTV is not stable in the body and may move due to internal organ movements. Considering the possible motions, a motion safety margin should be determined and drawn around the CTV to form the ITV. ITV is already stable within the patient's body, but the manual re-positioning of the patient during day-by-day treatment schedule is only possible with certain errors. Therefore, the daily setup error should be taken into account with a safety margin drawn around the ITV to form the final planning volume, i.e. the PTV. Only the full therapeutic dose of PTV provides the treatment of the real tumorous region: the CTV.

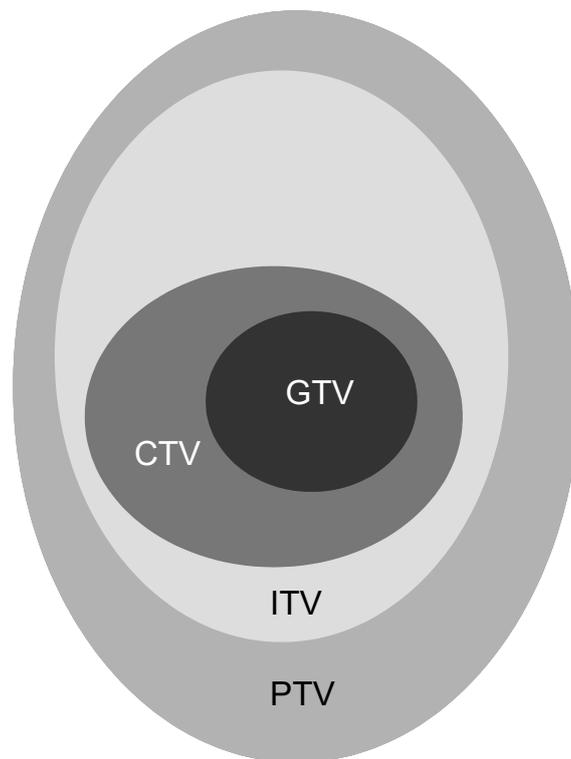


Figure 5: target volumes³

It can be seen that due to the applied safety margins, many normal tissues have to be irradiated, which increases the risk of unwanted side effects. Therefore, efforts should be made to use the smallest possible safety margins.

4. Definition of safety margins

4.1. The motion safety margin (CTV \rightarrow ITV)

The nature and extent of the internal organ movement that causes the CTV to change position must be taken into account when determining the motion safety margin.

Movement of CTV can be cyclical and random. For example, a pulmonary tumour moves cyclically when breathing. For example, a prostate tumour may move randomly due to saturation and movement of the bladder and the rectum.

Different degrees of displacement can be expected in different directions. A mediastinal tumour moves more posteroanteriorly, whereas a lower-lobe tumour moves more caudocranially with breathing.

The extent of movement depends greatly on the location of the CTV within the body. With a cranial lesion, there is virtually no movement, while a lung, liver or kidney tumour can move at several centimetres in amplitude.

Clinical research on the extent of movement can be found in many places in the literature.^{4,5,6,7,8,9,10}

4.2. The setup safety margin (ITV \rightarrow PTV)

The patient should be positioned on the treatment table every day during treatment in the position in which he or she was lying during CT scan for target volume determination and radiation planning. In practice, positioning reproducibility is facilitated by tailor-made patient positioning devices (headrests, armrests, foot, knee and arm restraints, customized thermoplastic masks, vacuum mattresses, etc.), but a few millimetres setup error appear in almost every positioning case.

The average of the daily set-up errors are called systematic error and is denoted by Σ . Ideally, the systematic error is zero. In practice, this is usually not the case. The average deviation of the daily adjustment errors from Σ is called a random error and is denoted by σ .

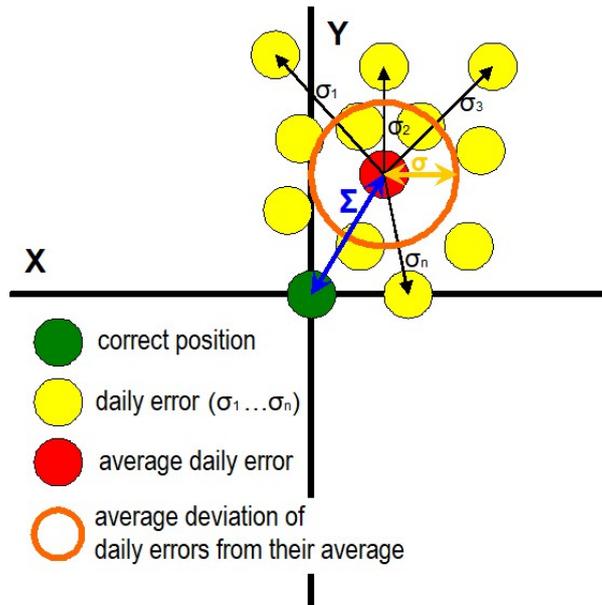


Figure 6: systematic and random error³

The applicable set-up margin should be determined as the weighted sum of systematic and random errors, taking into account the relevant Σ and σ values for the treatment of the individual patient.¹¹ The magnitude of Σ and σ depends on the device used to facilitate the placement, the positioning technique, the treatment region and the geometry of the patient. If Σ and σ are values for a disease type, treatment methodology, layout, device used, etc. already known in a particular therapeutic center, the following formula can be used generally, with sufficient accuracy, where M is the measure of the applicable safety margin to ensure that at least 90% of patients receive a minimum dose of 95% of the prescription dose:¹²

$$M = 2.5\Sigma + 0.7\sigma$$

Thus, the setup margin is affected by a systematic error 3.6 times more than a random error. Therefore, the main priority should be to reduce this one. There are several remediation strategies that fall into two main groups.

5. IGRT protocols

5.1. The on-line IGRT

The first group is the so-called on-line correction strategy, which involves determining the amount of misalignment before each treatment day and adjusting the patient's position by moving the table top. Thus, in addition to eliminating a systematic error, a random error can also be corrected. The degree of motion safety margin to be applied depends only on the accuracy of the device used to determine the positioning error. With today's technical capabilities, the resulting inaccuracy is one order of magnitude smaller than the corrected error itself.

The disadvantage of this procedure is that the patient receives dose exposure during imaging in addition to the therapeutic dose every day. Although this is two orders of magnitude less than the fractional dose obtained during treatment, it must be kept in mind.

5.2. Off-line IGRT

The second group consists of off-line correction strategies. Their advantage is that they require less time and workload compared to the online protocol, but do not allow the correction of random errors. The reason for this is that off-line protocols do not necessarily have to be captured every day of treatment, which requires less work, but loses the ability to collect information on a daily basis. Off-line protocols are also well suited for reducing systematic setup error. Various off-line correction strategies are described in several places in the literature.^{13,14,15,16}

5.2.1. NAL protocol

One of the off-line strategies is the Non-Action Level (NAL) protocol. The patient's position is recorded on the first three days of treatment, but the position is not corrected on these days. At the end of the third day, the recordings are analysed and the average adjustment error is calculated from the records. This mean value is used for subsequent treatment days as the required correction shift. No further images will be captured during treatment.

The advantage of this method is that it requires little imaging time and the images are analyzed afterwards the treatment, so that the total daily treatment time is not increased. The disadvantage is that the systematic error is determined from a limited number of measurements and there is no post verification of its correctness, so this error type is only partially corrected. In order to reduce the risks of this feature, it is customary to take a weekly

check, and if you experience a setup error greater than the specified tolerance, restart the three-day recording cycle and calculate a new average. A further disadvantage of the method is that it cannot reduce the random error at all.

The flowchart of the NAL protocol is as follows:

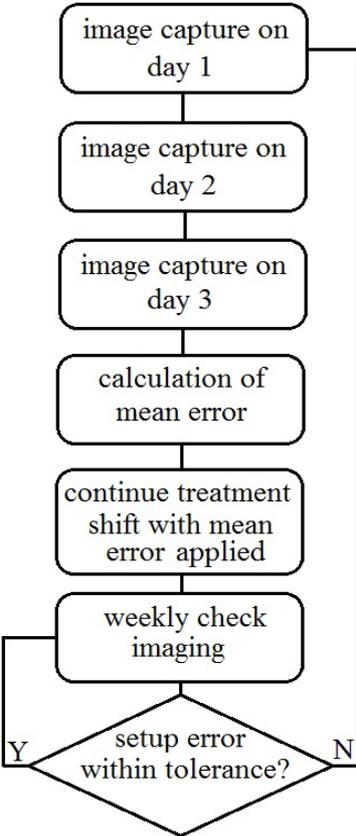


Figure 7: NAL protocol

5.2.2. SAL protocol

Another off-line strategy is the Shrinking Action Level (SAL) protocol. In essence, a picture is taken on the treatment day and then compared the ratio of a predetermined limit of α divided by the square root of the treatment day (n_i) resulting in the daily error found on the recording (μ_{SAL}). If the quotient remains below the intervention level, the next day we will record again and repeat the calculation and comparison, but this time the treatment number is increased by one. Thus, as treatment days progress, an increasingly stringent intervention level is applied. If the calculated daily error is greater than the intervention level for that day, the patient's position is adjusted and the treatment day indicator is reset. If adjustment had not been needed any time until the predetermined n_{max} record number (treatment day) was reached, the

record sequence is interrupted and no recordings are made for the remainder of the treatment. The flowchart for the SAL protocol is as follows:

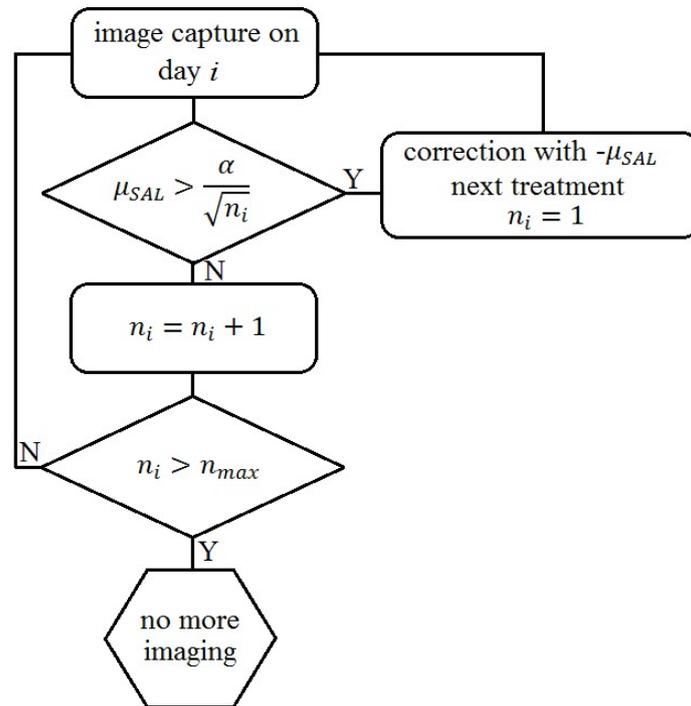


Figure 8: SAL protocol

By choosing α and n_{max} it is possible to influence the extent of systematic error reduction and the amount of work required.

The advantage of this method is that it eliminates the premature adjustment error correction, which would be based on the first few measurements when the errors are still largely due to random errors rather than systematic errors.

The disadvantage is that its efficiency is limited, because when the recording cycle is restarted, information from previous recordings is lost.

The setup margin can be reduced by applying on-line or off-line adjustment strategies. The practical application of these techniques requires the use of imaging technology and equipment.

6. Organ motion monitoring

We've covered the setup margin above, but it's also an important issue to reduce the motion safety margin. The latter is made possible by treatment management based on monitoring and tracking of organ movement.

6.1. Respiratory gating

Gating is used when the tumor to be irradiated moves at a rate consistent with some periodic repetitive internal organ movement. The most typical examples are small solitary tumor nodules located in the lower and outer peripheral areas of the lungs and in the liver or pancreas. These are usually not primary tumors but metastases and are treated in fractions 5-7 with a dose of 7-12 Gy. If such a target are having a motion of up to 2-3 cm in diameter and with an amplitude of 1.5-2 cm were continuously radiated during motion, the size of the motion safety margin to be selected would be commensurate with the diameter of the target point. At this time, we would radiate 2-3 times the volume required, half and two-thirds of which is actually normal tissue.

To avoid this, the tumor is irradiated at a selected position only during a specific phase of the motile airway. This is done by monitoring free breathing and gating on the basis of the breathing curve. That is, the beam is only turned on when the tumor is in the correct position. By observing the rise and fall of an object reflected in the infrared range on the chest of a lying patient, it is possible to record a breathing curve using an infrared camera. The camera and its software are connected to the irradiation device. In this way, it is possible to control the irradiation, interrupt the radiation beam, and gate, based on the signals coming from the infrared camera, that is, the movement of the patient's chest. The figure below shows such an infrared camera system.

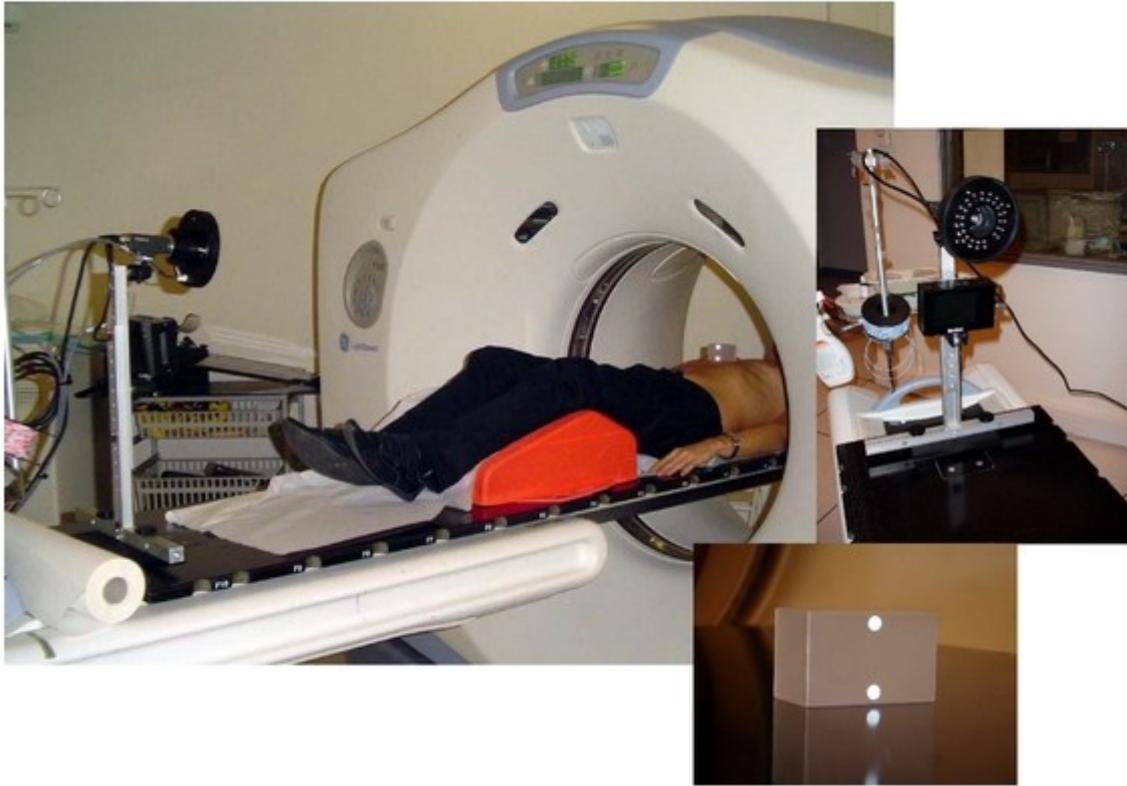


Figure 9: respiratory gating infrared camera system¹⁷

A 4D CT scan is needed to assess tumor movement as early as radiation planning. This is a set of 10 CT scans that can be played back in motion. This is used to determine the target amplitude of deflection and the respiratory phase (or phases) in which the irradiation will be performed. By connecting the above-mentioned infrared camera system to the CT device, the breathing phase can be assigned to each other at the moment.

In total, therefore, multiple sequential CT scans are performed to monitor the patient's respiratory rate to determine the irradiation phase. CT scans at the selected phase are used for the treatment planning. Breathing is again monitored during the treatment and the beam is gated to the prescribed phase. This reduces the required motion safety margin and saves a considerable volume of normal tissue.

6.2. Marker tracking

The purpose of the Marker tracking procedure is similar to that of the respiratory gating, which is to reduce the motion safety margin caused by CTV displacement by internal organ movements. It has a periodic, predictable pattern of respiration, and non-invasive modifications can be observed with great precision. However, there are organ-induced motions that of occurrence times and the extent of evasion are random. The most common

example is the prostate, a target area of up to 1.5 to 2 cm, due to a sudden change in rectum filling.

Movement of the prostate is not visible outside the patient's body. Therefore, permanent metal markers are implanted in the prostate prior to the planning CT scan. Minimum 3, gold or other, biologically non-active metal are used as in other fields of medicine. They are not larger than one grain of wheat.

During the irradiation, the position of the markers is monitored by continuous low energy X-rays independent of the therapeutic beam. Using a computer, continuous comparisons are made: the reference position calculated from the planning CT scan and the current marker positions are compared. If the markers (and the prostate that carries them) move out, the radiation will stop immediately. At this point, the patient is repositioned, the distended prostate is returned to the desired position. Radiation and observation then can be continued. The X-ray image of the implanted markers in the prostate is shown below.

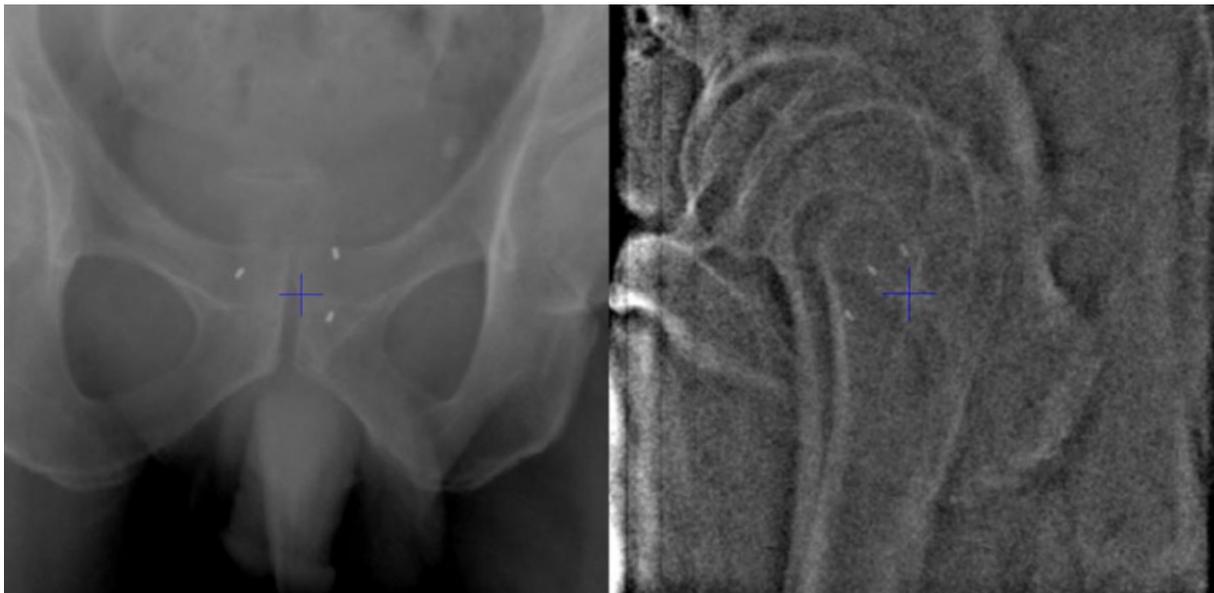


Figure 10: fiducial markers in the prostate¹⁸

There is also a technology in which tiny radio frequency transmitters (RFIDs) are implanted into the prostate, not metal markers. Their movement can be tracked with a radio transceiver placed over the patient's skin, eliminating the need for low-energy X-ray imaging and the accompanying dose.

6.3. Surface matching

The surface matching method can be used when the target volume and the patient's external skin surface cannot move due to anatomical fixation. A good example is a tumor in the cranial space that does not move relative to the face and scalp.

Planning CT images determine where the patient's external skin contour is positioned and at what angle to the isocentre of the irradiation device it is laying to. This is the reference situation. During treatment, the patient's true external contour is monitored by a dual camera system. Based on the visual information from the two viewpoints, the spatial position of the skin surface shell can be computer-mapped. In this way, a surface-to-surface reconstruction can be made, which is compared with the reference situation. When the displacement exceeds the predetermined tolerable level during treatment, the irradiation may be interrupted and the patient may be repositioned if necessary. The system is shown in the figure below.

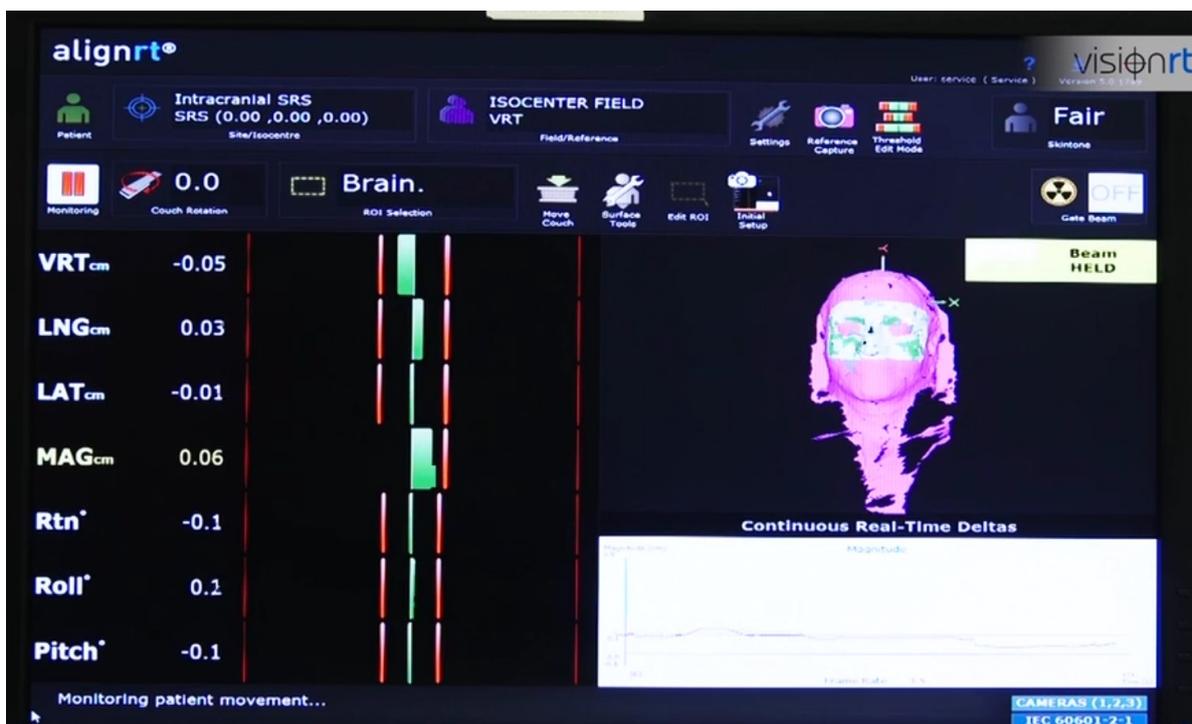


Figure 11: surface matching system¹⁹

7. Technology for image-guided radiation therapy

Imaging-guided radiation therapy (IGRT) is a method of correcting a patient's position and / or regulating the course of radiation therapy using an imaging modality.

7.1. Traditioan X-ray image

The simplest forms of IGRT date back to the 1970s and 1980s. The patient's position with respect to the beam was then checked with a traditional X-ray film. ^{20,21,22,23}

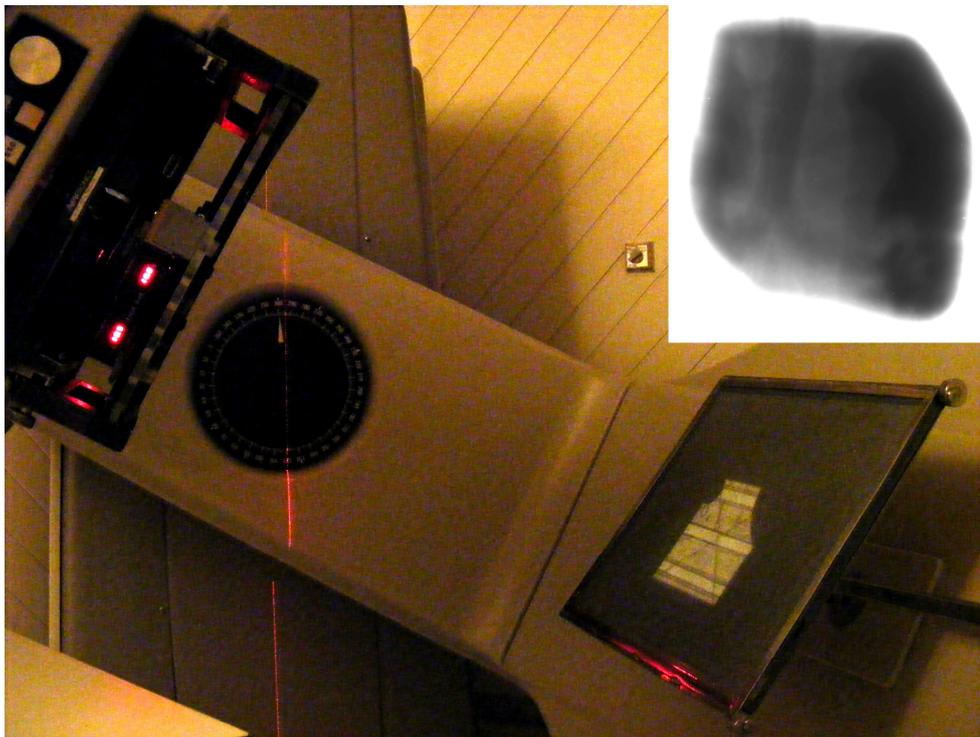


Figure 12: position verification with X-ray film³

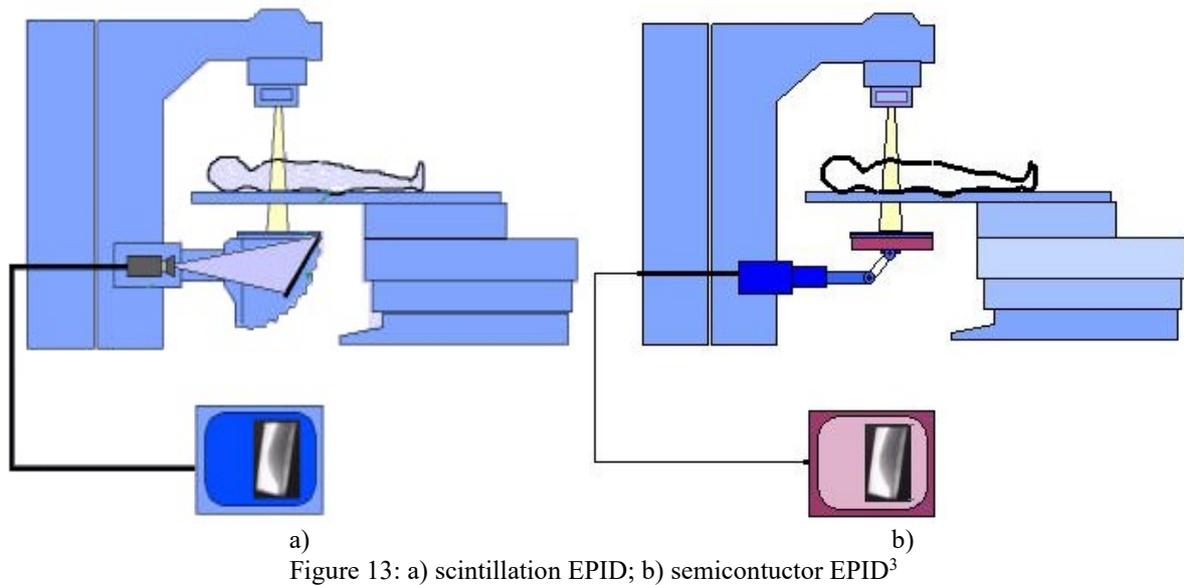
It was possible to determine which anatomical structures were in the path of the beam, and if necessary, position correction could be performed manually. The advantage of this technique is that high-quality, high-resolution images can be taken in the X-ray and orthovolt energy ranges. The disadvantage, however, is that it takes several minutes to develop the film, which is time consuming, requires new film for each recording, and therefore expensive, and difficult to evaluate in the megawatt energy range due to manual correction.

7.2. EPID

In the 1990s, with the advent of linear accelerators, scintillation detector portal image acquisition (EPID) devices appeared. ^{24,25,26}

High-energy X-rays produce light flashes on a scintillation plate mounted perpendicular to the direction of the radiation field, the intensity of which is proportional to the intensity of the X-rays they cause. A reflection mirror projects flashes of light into an optical camera, which transmits the analog image signal thus produced to the processing computer. This is where the image is digitized and its quality enhanced by software. It has the advantage that in this enhanced image the bony structures can be identified in an acceptable manner. It is also possible to determine the position of the soft tissues if a permanent marker marker is to be applied in advance (eg in case of prostate cancer).²⁷ The positioning error is determined by reference software (DRR) using computer software, therefore accuracy is higher than film technology, by a few millimeters. A further advantage is that it is possible to take a series of images during irradiation since the image is taken with the therapeutic beam. The disadvantage is that, despite its digitalization, its accuracy is limited by its analogue nature. The recording devices (scintillation plate, camera) become obsolete with regular use, so regular calibration or replacement is required.

In the early 2000s, with the advancement of semiconductor technology, semiconductor detector EPID devices appeared with the same field of use as their predecessor scintillation detector EPID. The semiconductor detector panel is mounted directly below the scintillation plate so that the image is digitized locally, so that the optical and electronic noise generated by the mirror and the camera does not degrade the image quality. However, digital image enhancement is still happening here. You get a high quality, sharp image. It is also possible to record a series of images. Positioning accuracy is better than the previous one, but still in the millimetre range. The position of the soft tissues can still be determined only with marker markers. The control electronics of the detector panel are very sensitive. If exposed to high-energy radiation, it can be easily damaged, so use of the device requires great care or software protection, which prevents the radiation from being triggered when the beam falls on the control electronics.



7.3. Ultrasound

The need for soft tissue positioning necessitated the development of a device capable of performing this task without the use of a marker. Ultrasonic BAT system allows to determine target volume displacement due to internal organ movement without using ionizing radiation.



The disadvantage is that for proper image quality the transducer needs to be clamped to the patient, and the resulting pressure itself can cause organ movement. Therefore, in order to avoid misidentification, the recruiter should have extensive experience. This technology is available but is not widespread.

7.4. X-ray image pair

The use of kilovolt imaging devices in radiotherapy also made it possible to display soft tissue better. An orthogonal verification system independent of the moving elements of the linear accelerator enables the position of the patient to be corrected to a few tens of millimetres. Imaging is done with two or four X-ray sources mounted on the floor or ceiling, and with digital detector panels facing them.



Figure 15: orthogonal X-ray verification³

Such a system is used primarily in stereotactic radiation therapy and radiosurgery, where small target volume size and proximity of organs to be protected require submillimetre precision. ^{28,29,30,31}

7.5. CT

With the tools described so far, two-dimensional or quasi-three-dimensional (two-dimensional processing of two 2D images) imaging can be performed, and based on the information obtained, three or six degrees of freedom (three translations + three rotations) allow patient position correction. Real three-dimensional volumetric imaging can be achieved by using computer tomography (CT) devices within the irradiation bunker with a linear accelerator in a coordinate system. There are three different technological implementations.

7.5.1. CT-on-rail

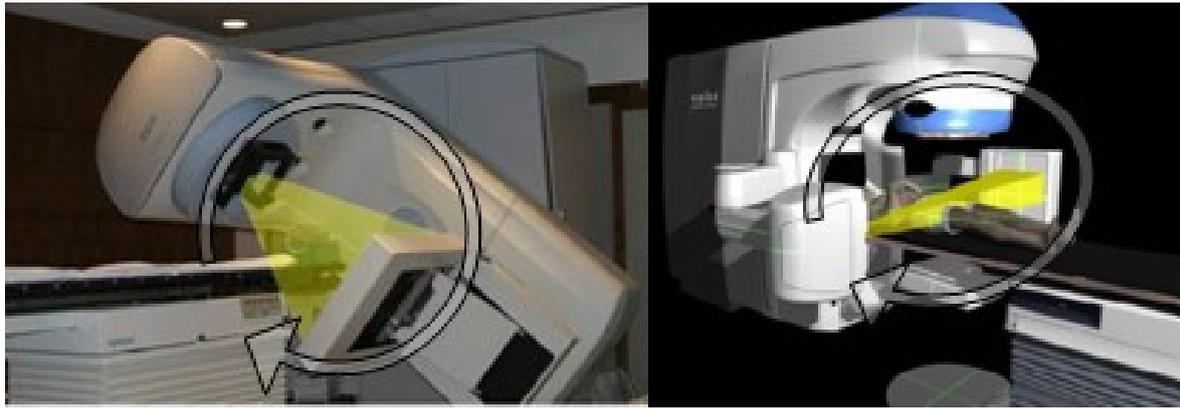
If the irradiation bunker can be used for diagnostic purposes, with a conventional CT device that can move on rails, is called CT-on-rail technology.³² Patient treatment couch rotates 180° with linear accelerator on one end and CT-on-rail on the other. During imaging, the CT unit performs linear movement on the rails in a straight line, while the desk table is motionless. The method is very space-consuming and its accuracy is limited by the uncertainty of stability of the rotational axis of the control table. The advantage is that the diagnostic CT can work with very good imaging quality. However, due to its disadvantages, the method is less widespread.

7.5.2. Conebeam CT

Commonly used devices are megavolt (MV) and kilovolt (kV) Cone-beam CT (CBCT). In both cases, a CT scan is made by rotating the linear accelerator completely or partially once. In MV case, high energy therapeutic beam and semiconductor detector EPID device are used for imaging.^{33,34,35} For kV CBCTs currently in clinical use, an imaging field perpendicular to the main axis of the therapeutic beam is used.^{36,37,38}



a)



b) c)
Figure 16: a) CT-on-rail; b) MV and c) kV ConeBeam CT³

The advantage of the MV method is that only one image processing software is required along with the EPID, while in the kV case, one X-ray source and another semiconductor detector capture panel. In MV, the identity of the therapeutic and imaging radiation fields can increase accuracy, but the MV beam allows for lower quality soft tissue imaging than kV, where the difference between the centers of rotation of the two radiation fields can cause positioning errors.³⁹ Metal implants in the patient's body produce imaging artifacts in the kV case, which is not significant in MV. The concomitant dose is higher with MV imaging than with kV. It can be seen that both systems have advantages and disadvantages.⁴⁰ In practice, however, the kV system is more widespread. There may also be a combination of the two systems.⁴¹

It is also possible to combine CBCT with respiratory gating. This is used when the target volume performs periodic movement as a result of breathing. Treatment is based on a 4D CT irradiation plan, so positioning must also be 4D CBCT based. The correct position is determined in the selected breathing phase. Reference 4D CT and 4D CBCT are compared in this phase.

A literature report is available on the results of comparing the accuracy of the kV CBCT with the orthogonal X-ray verification device. It has been established that the latter, if used with due caution, may constitute an alternative to the former.⁴²

Imaging-guided radiotherapy devices are not only capable of measuring and correcting patient positioning errors. Some of these can be used successfully to monitor internal organ motion and thereby control therapeutic radiation.^{43,44} A detailed description of these systems is given in chapter 6

8. Remarks

The need for image-guided radiotherapy and the need to monitor and correct patient position is an integral part of quality radiotherapy. In recent decades, as technology has advanced, more and more accurate and efficient methods have emerged. The increase in the performance of computers over the last ten years has brought about an explosive development, and imaging is no longer just a control function, but in many cases an indispensable security procedure. The widespread use of image-guided radiotherapy techniques reduces the setting and a movement safety margin used in target volume determination and reduces the dose burden on organs-at-risk. Ultimately, it can improve treatment efficiency and reduce the likelihood of unwanted side effects. All these may serve as a basis for the development of new radiotherapy methods and alternative dosage regimens. Nowadays, a modern radiotherapy centre cannot afford to work without image-guided radiotherapy.

Literature

- 1 Laurent C. Tantot: Modelling ionisation chamber response to nonstandard beam configurations. Medical Physics Unit, McGill University, Montreal, 2007.
- 2 International Commission on Radiation Units and Measurements (ICRU) Report 50 and 62, Prescribing, Recording and Reporting Photon Beam Therapy. ICRU News 1993-1999.
- 3 Kovács P, Sebestyén Zs, Farkas R, et al. A képzérezelt sugárterápia formái és alkalmazása. EGÉSZSÉG-AKADÉMIA 2010. 313-322.
- 4 Keros L, Bernier V, Aletti P, et al. Qualitative estimation of pelvic organ interactions and their consequences on prostate motion: Study on a deceased person. Med Phys 2006; 33:1902-1910.
- 5 Zelefsky MJ, Crean D, Mageras GS, et al. Quantification and predictors of prostate motion variability in 50 patients evaluated with multiple CT scans during conformal radiotherapy. Radiother Oncol 1999; 40:129-133.
- 6 Rosewall T, Chung P, Bayley A, et al. A randomised comparison of interfraction and intrafraction prostate motion with and without abdominal compression. Radiother Oncol 2008; 88:88-94.
- 7 Rimmer YL, Burnet NG, Routsis DS, et al. Practical issues in the implementation of image-guided radiotherapy for the treatment of prostate cancer within a UK department. Clin Oncol 2008; 20:22-30.
- 8 Jereczek-Fossa BA, Cattani F, Garibaldi C, et al. Transabdominal ultrasonography, computed tomography and electronic portal imaging for 3-dimensional conformal radiotherapy for prostate cancer. Strahlenther Oncol 2007; 183:610-616.
- 9 Qi XS, White J, Rabinovitch R, et al. Respiratory organ motion and dosimetric impact on breast and nodal irradiation. Int J Radiat Oncol Biol Phys 2010; 78:609-617.
- 10 Kovacs A, Hadjiev J, Lakosi F, et al. Dynamic MR based analysis of tumor movement in upper and mid lobe localized lung cancer. Pathol Oncol Res 2009; 15:269-277.
- 11 Stroom JC, de Boer HCJ, Huizenga H, et al. Inclusion of geometrical uncertainties in radiotherapy treatment planning by means of coverage probability. 1999; 43:905-919.
- 12 van Herk M, Remeijer P, Rasch C, et al. The probability of correct target dosage: dose-population histograms for deriving treatment margins in radiotherapy. Int J Radiat Oncol Biol Phys 2000; 47:1121-1135.
- 13 Bel A, van Herk M, Bartelin H, et al. A verification procedure to improve patient set-up accuracy using portal images. Radiother Oncol 1993; 29:253-260.

-
- 14 De Boer JCJ, Heijmen BJM A protocol for the reduction of systematic patient set-up errors with minimal portal imaging workload. *Int J Radiat Oncol Biol Phys* 2001; 50:1350-1365.
 - 15 Bel A, Vos PH, Rodrigues PT, et al. High-precision prostate cancer irradiation by clinical application of an off-line patient set-up correction procedure, using portal imaging. *Int J Radiat Oncol Biol Phys* 1996; 35:321-332.
 - 16 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; 67:1586-1595.
 - 17 Giraud P, Houle A. Respiratory Gating for Radiotherapy: Main Technical Aspects and Clinical Benefits. *ISRN Pulmonology* 2013; ID 519602
 - 18 Ng M1, Brown E, Williams A, et al. Fiducial markers and spacers in prostate radiotherapy: current applications. *BJU Int.* 2014; 113 Suppl 2: 13-20.
 - 19 Vision RT website: www.visionrt.com/technology/surface-guided-radiation-therapy
 - 20 Roth RJ. Megavolt portal radiography using film and xerox techniques. *Radiol Technol* 1964; 36:65-69.
 - 21 Galkin BM, Wu RK, Suntharalingam N. Improved technique for obtaining teletherapy portal radiographs with high-energy photons. *Radiology* 1978; 127:828-830.
 - 22 Keller BE. Electron-beam radiographs. *Radiology* 1978; 128:830-831.
 - 23 van Arsdale E. Simple modification of a radiation therapy table for portal film radiographs. *Radiol Technol* 1983; 54:476-478.
 - 24 van Tienhoven G, Lanson JH, Crabeels D, et al. Accuracy in tangential breast treatment set-up: a portal imaging study. *Radiother Oncol* 1991; 22:317-322.
 - 25 el-Gayed AA, Bel A, Vijlbrief R, et al. Time trend of patient setup deviations during pelvic irradiation using electronic portal imaging. *Radiother Oncol* 1993; 26:162-171.
 - 26 Hunt MA, Schultheiss TE, Desobry GE, et al. An evaluation of setup uncertainties for patients treated to pelvic sites. *Int J Radiat Oncol Biol Phys* 1995; 32:227-233.
 - 27 Vigneault E, Pouliot J, Laverdière J, et al. Electronic portal imaging device detection of radioopaque markers for the evaluation of prostate position during megavoltage irradiation: a clinical study. *Int J Radiat Oncol Biol Phys* 1997; 27:449-454.
 - 28 Jin JY, Yin FF, Tenn SE, et al. Use of the BrainLAB ExacTrac X-Ray 6D system in image-guided radiotherapy. *Med Dosim* 2008; 33:124-134.

-
- 29 Wurm RE, Erbel S, Schwenkert I, et al. Novalis frameless image-guided noninvasive radiosurgery: initial experience. *Neurosurgery* 2008; 62:A11-17; A17-18.
 - 30 van Santvoort J, Wiggenraad R, Bos P. Positioning accuracy in stereotactic radiotherapy using a mask system with added vacuum mouth piece and stereoscopic X-ray positioning. *Int J Radiat Oncol Biol Phys* 2008; 72:261-267.
 - 31 Takakura T, Mizowaki T, Nakata M, et al. The geometric accuracy of frameless stereotactic radiosurgery using a 6D robotic couch system. *Phys Med Biol* 2010; 55:1-10.
 - 32 Oita M, Takegawa Y, Yagi H, et al. Quality control (QC) of CT on rail system (FOCAL Unit) with a micro-multi leaf collimator (mMLC) using new GafChromic film for stereotactic radiotherapy. *Nippon Hoshasen Gijutsu Gakkai Zasshi* 2006; 62:711-713.
 - 33 Ford EC, Chang J, Mueller K, et al. Cone-beam CT with megavoltage beams and an amorphous silicon electronic portal imaging device: potential for verification of radiotherapy of lung cancer. *Med Phys* 2002; 29:2913-2924.
 - 34 Seppi EJ, Munro P, Johnsen SW, et al. Megavoltage cone-beam computed tomography using a high-efficiency image receptor. *Int J Radiat Oncol Biol Phys* 2003; 55:793-803.
 - 35 Morin O, Gillis A, Chen J, et al. Megavoltage cone-beam CT: system description and clinical applications. *Med Dosim* 2006; 31:51-61.
 - 36 Jaffray DA, Siewerdsen JH, Wong JW, et al. Flat-panel cone-beam computed tomography for image-guided radiation therapy. *Int J Radiat Oncol Biol Phys* 2002; 53:1337-1349.
 - 37 McBain CA, Henry AM, Sykes J, et al. X-ray volumetric imaging in image-guided radiotherapy: the new standard in on-treatment imaging. *Int J Radiat Oncol Biol Phys* 2006; 64:625-634.
 - 38 Oelfke U, Tücking T, Nill S, et al. Linac-integrated kV-cone beam CT: technical features and first applications. *Med Dosim* 2006; 31:62-70.
 - 39 Sharpe MB, Moseley DJ, Purdie TG, et al. The stability of mechanical calibration for a kV cone beam computed tomography system integrated with linear accelerator. *Med Phys* 2006; 33:136-144.
 - 40 Korreman S, Rasch C, McNair H, et al. The European Society of Therapeutic Radiology and Oncology-European Institute of Radiotherapy (ESTRO-EIR) report on 3D CT-based in-room image guidance systems: a practical and technical review and guide. *Radiother Oncol* 2010; 94:129-144.

-
- 41 Wertz H, Stsepankou D, Blessing M, et al. Fast kilovoltage/megavoltage (kVMV) breathhold cone-beam CT for image-guided radiotherapy of lung cancer. *Phys Med Biol* 2010; 55:4203-4217.
- 42 Chang Z, Wang Z, Ma J, et al. 6D image guidance for spinal non-invasive stereotactic body radiation therapy: Comparison between ExacTrac X-ray 6D with kilo-voltage cone-beam CT. *Radiother Oncol* 2010; 95:116-121.
- 43 Wurm RE, Gum F, Erbel S, et al. Image guided respiratory gated hypofractionated Stereotactic Body Radiation Therapy (H-SBRT) for liver and lung tumors: Initial experience. *Acta Oncol* 2006; 45:881-889.
- 44 Willoughby TR, Forbes AR, Buchholz D, et al. Evaluation of an infrared camera and X-ray system using implanted fiducials in patients with lung tumors for gated radiation therapy. *Int J Radiat Oncol Biol Phys* 2006; 66:568-575.