Chapter 2
Motion Compensation in Robotic Radiosurgery

This chapter describes the principles of motion compensation in radiotherapy with a focus on robotic radiosurgery, starting with a brief description of the medical implications. Throughout, special emphasis will be placed on the CyberKnife® system and we will outline the problems originating from the aim of real-time motion compensation. The main current application of robotic radiotherapy is the treatment of malignant tumours while a second, very promising field is the therapy of cardiac arrhythmia, especially of atrial fibrillation. An outline of this project called CyberHeart, and the challenges emanating from it, will be given in section 2.5.

2.1 Medical Implications

As a fully automatic system designed to compensate for respiratory and pulsatory motion as well as for motion of the patient, the CyberKnife (and also the CyberHeart extension) allows for treatment of cancerous regions anywhere in the body. Especially important, due to the system's possible sub-millimetre accuracy [19, 48], the treatment of previously inoperable or surgically complex tumours has become possible, opening up a new treatment option for a great multitude of patients.

The aforementioned problem of latency, however, as well as the notoriously difficult task of determining organ motion using non-invasive imaging methods, is responsible for the remaining inaccuracies and limitations of the system. Especially in those cases where tumour motion is large (i.e. tumours in the central lung or tumours close to the diaphragm) and respiration of the patient is irregular, targeting accuracy might be compromised. Consider the situation depicted in figure 2.1: the clinician determines the cancerous area to be treated (called Gross Tumour Volume (GTV)). This area is expanded to include regions where the cancer might have already spread to, i.e., regions where some cells are cancerous. This is called the Clinical Target Volume (CTV), which is further enlarged to cover imaging and treatment uncertainties (then called Planning Target Volume (PTV)). Usually, certain areas of the body are classified as Organ at Risk (OAR), i.e. regions which should be spared from irradiation.
tion as much as possible. If planning of the radiosurgical treatment is done at one phase of respiration (e.g. on a breath-hold Computed Tomography (CT) scan) and the treatment is delivered while the patient is breathing freely, the treatment beams might not be placed as planned (figure 2.1).

![Fig. 2.1: (a) Typical situation of an Organ at Risk (OAR), the Gross Tumour Volume (GTV) and the Planning Target Volume (PTV) (b) Two treatment beams are shown during one respiratory phase (c) The same treatment beams can hit the OAR during another respiratory phase or might miss the GTV](image)

As a consequence, the PTV is usually selected much larger than clinically required to cope with these inaccuracies. Clearly, this artificial enlargement as well as the inevitable blurring of the dose gradients due to organ motion render certain tumours intreatable without motion compensation. Subsequently, when the OARs are too close to the GTV, the enhanced margin required for Conformal Radiation Therapy (CRT), 3D Conformal Radiation Therapy (3DCRT) and other approaches not compensating for motion, can cause severe difficulties when creating the treatment plan. These difficulties can even be so grave that accurate planning and treatment is not possible, not because the GTV cannot be dealt with, but because the OARs would be in too great danger.

### 2.2 Active Tumour Tracking in Image-Guided Radiotherapy

#### 2.2.1 The CyberKnife

The first system intended to accurately treat tumours anywhere in the human body has been developed from 1987 on by Dr. John R. Adler, Jr., at Stanford University. It was envisioned in [15, 16], initially called ADLR [2] and then Neurotron 1000 [5, 32] and intended for stereotactic radiosurgery of brain tumours. It was first used clinically on June 8, 1994 [3, 63]. The system was subsequently renamed CyberKnife and has been further improved by a collaboration of American and German scientists [4, 6, 7, 10, 41–47]. The system has since been manufactured commercially by Accuray, Inc.,(A) and received U.S. Food and Drug Administration (FDA) approval for treatment of stationary tumours (head, neck and upper spine) in 1999.
2.2 Active Tumour Tracking in Image-Guided Radiotherapy

Fig. 2.2: The CyberKnife® (copyright Accuray, Inc.). The figure shows the robotic arm (left) carrying the linear accelerator, the ceiling-mounted X-ray sources, the X-ray detectors (the flat panel on the room’s floor), the optical tracking device (ceiling-mounted, on the right) and a patient equipped with the Synchrony® vest on the robotic couch.

Fig. 2.3: Vest with Synchrony® markers (copyright Accuray, Inc.). Note that the markers can be placed nearly anywhere on the patient’s chest.
and for all other body parts in 2001. The system also allows for irradiation of tumours which move with respiration by compensating for this motion. The so-called Synchrony® respiratory tracking system was approved by the FDA in 2004. The current generation of the CyberKnife is shown in figure 2.2.

The system consists of a standard six-jointed industrial robot, the medical version of the KUKA KR 240(B), which carries a lightweight Linear Accelerator (LINAC) to generate the treatment beam. The robot is used to position the LINAC at multiple positions around the patient to ensure homogeneous coverage of the tumour with steep dose gradients. Furthermore, the robotic system allows for near real-time compensation of target motion.

The general concept of the CyberKnife is to

- manually delineate tumours in a pre-operative CT scan, to
- create a treatment plan, then to
- match the CT to the position of the patient during treatment, and
- update and correct the positioning to ensure accurate delivery of the prescription dose [62].

The target’s position is determined using stereoscopic X-ray imaging of either bony structures [35], clearly visible tumours [45], or artificial landmarks [44], so-called fiducials. Typically, the fiducials are gold rods of 3-5 mm length and 0.5-2 mm diameter. In the case of breath-dependent tumours, an external surrogate signal is used to fill the gaps between the acquisition of X-ray shots, which are taken at irregular intervals, to minimise the radiation dose from imaging. This signal is acquired at approximately 27 Hz with the FlashPoint 5500 (Stryker, Inc.) tracking system capable of detecting optical markers. These optical markers are placed on the patient’s chest and allow for precise tracking of respiratory motion. A typical setup is shown in figure 2.3.

The procedure of treating breath-dependent tumours can be described as follows:

- The tumour is localised and delineated on a pre-treatment CT scan. In certain cases, fiducials are implanted under CT guidance.
- The patient is placed on the treatment couch and, using stereoscopic X-ray imaging, is registered to the CT scan.
- A correlation model relating the surrogate signal (optical markers on the patient’s chest) to the tumour motion is built using several X-ray images.
- The LINAC is placed on predetermined positions to deliver the required radiation dose to the tumour.
- Motion of the patient is monitored by optical tracking and automatically compensated by moving the LINAC. The validity of the correlation model between optical marker motion and tumour motion is checked regularly and the model is updated accordingly.

Figure 2.4 shows a sketch of the principles of robotic radiosurgery. It is important to note that internal organ motion will not be the same as external motion.
In contrast to moving the LINAC with a robotic arm, two other methods to actively compensate for tumour motion have been devised recently. One is based on moving the patient with a robotised treatment couch [11, 12, 65], the second is based on moving the LINAC using a gimbals approach [18, 22, 60]. The couch method has, until today, not reached clinical practice, whereas the gimbals approach has just been started to be manufactured commercially by Mitsubishi Heavy Industries Medical Systems, Inc., (D) as MHI-TM2000. It is distributed outside Japan by BrainLAB AG (E) as the VERO High Precision Radiation Therapy System. It is based on a gimbled X-ray head and C-band LINAC, both mounted in an O-ring. Using the gimbals mount, the LINAC can easily be moved in two Degrees of Freedom (DOF), the other two relevant DOFs are realised by rotating the O-ring or by skewing the O-ring around its base. Additionally, the patient is set up by means of a motorised couch and the beam can be shaped using a Multi-Leaf Collimator (MLC). The device is shown in figure 2.5. To date, the MHI-TM2000 system has been installed at two Japanese and one overseas site (Brussels University Hospital) [34] where it went operational on 27.11.2009 [61].

Two other methods, which do not directly move the beam source, are also currently under development. The first involves dynamic adaptation of the treatment beam’s shape during irradiation. This method, known as Dynamic Multi-Leaf Collimator (DMLC) [24, 30, 31, 38] or Synchronised Moving Aperture Radiation Therapy (SMART) [36, 67], will be covered in section 2.3. The other method tries to incorporate motion information into the delivery of tomotherapy treatment plans, a method called Motion-Adaptive Delivery (MAD). Tomotherapy devices are also described in section 2.4.
2.3 Gantry-Based Systems

In contrast to robotic systems actively compensating for motion, like the CyberKnife, or the new O-ring based MHI-TM2000/VERO system, most commonly used radiotherapy devices are gantry-based. This means that the LINAC cannot move in four or more DOFs, but is mounted on a cylindrical assembly in the bore of which the patient is placed. Figure 2.6 shows two different gantry-based systems, being the Elekta\textsuperscript{(F)} Synergy\textsuperscript{®} S, \textit{figure 2.6a}, and the Varian\textsuperscript{(G)} Clinac, \textit{figure 2.6b}, systems. These systems usually only allow for rotation around their major axis while patient setup has to be done manually or using a motorised couch.

2.3.1 Respiratory Gating

The usual approach for gantry-based systems is to only irradiate the tumour during certain respiratory phases, e.g. during maximum exhalation. This method is called \textit{gating}. One of the first approaches to monitoring the motion of the target was Mitsubishi’s Real-Time Respiratory Tracking (RTRT) system. It is a gantry-based system using up to four room-mounted X-ray detectors to track the motion of fiducials implanted into the tumor. It has been first presented in 1999 \cite{54} and more detailed descriptions were given in 2000 \cite{52, 53}. The RTRT system is shown in \textit{figure 2.8}. This system, however, did not find wide acceptance, possibly due to the constant additional radiation from fluoroscopic tracking. Although this additional dose is not very high \cite{51}, it still seems to be a concern for most physicians, even more so since other, less invasive gating methods are commercially available. One such method is Varian’s Real-time Position Management System (RPM), which tracks the chest of a patient using an optical tracking system and an acrylic box with six markers (see \textit{figure 2.7a}). BrainLAB’s ExacTrac\textsuperscript{®} Adaptive Gating method works in a similar
2.3 Gantry-Based Systems

(a) Elekta’s Synergy S
(photograph courtesy of Elekta)
(b) Varian’s Clinac
(photograph courtesy of Varian Medical Systems)

Fig. 2.6: Classical gantry-based IMRT systems. Both systems feature an MV imager, the Synergy system also has an orthogonally mounted kV imager.

(a) Varian’s RPM system
(photograph courtesy of Varian Medical Systems)
(b) Elekta’s Active Breathing Coordinator
(photograph courtesy of Elekta)

Fig. 2.7: Commercially available respiratory gating devices
manner, but instead of relying on an external marker box, it uses a combination of stereoscopic X-ray imaging and infrared patient tracking.

Fig. 2.8: Mitsubishi’s RTRT system (photograph courtesy of Hiroki Shirato, Hokkaido University Hospital). Only three of the four X-ray imagers are visible.

A different approach to gating is followed by Elekta’s Active Breathing Coordinato

or™, which requires the patient to actively pause his breathing at pre-defined tidal volumes measured by an aeroplethysmograph. Treatment delivery is subsequently coordinated with this pause (see figure 2.7b) [66]. A similar approach, called Deep Inspiration Breath Hold (DIBH), requires the patient to exhale as much as possible. Gating is then performed at this tidal level [17, 39, 40].

2.3.2 Beam Shaping

The Novalis Tx™ system, manufactured by Varian in cooperation with BrainLAB, see figure 2.9, takes the classical gantry approach one step further by incorporating motion tracking capabilities similar to the CyberKnife system (including stereoscopic X-ray target localisation and respiratory gating). Additionally, it features MV- and kV-imaging as well as MV- and kV-CT. However, this device does not actively compensate for respiratory motion. Most such systems are based on the principle of Intensity Modulated Radiation Therapy (IMRT) [13, 20]. This method does not use the same beam size and shape throughout the treatment but modifies these parameters for each beam or even during the active time of individual beams. Such modification can be achieved by using

1 Novalis® is a trademark of Brainlab AG in Germany and the US.
an MLC [14, 59], a device consisting of multiple metallic leaves made of a high atomic numbered material (usually Wolfram) which can be moved in and out of the beam path to block or attenuate parts of the radiation. An alternative way to shape the beam in IMRT is using physical modulators or compensating filters [28]. Since using such filters is highly cumbersome, their use is not widely spread and they have been described as being an interim technology [20]. Two MLCs and a sketch detailing how the beam shape is modified in a clinical setting are shown in figure 2.10.

This is done to create irradiation fields of varying intensity, which are applied to the patient from different positions. Note that these fields do not necessarily conform to the form of the tumour as seen from the source of radiation (this is also called Beam’s Eye View (BEV)). Classically, MLCs were used for CRT and, subsequently, 3DCRT, to spare healthy tissue. They have been incorporated into IMRT planning [23] only recently when computational power became sufficiently high.

Using IMRT—as opposed to classical CRT—it has become possible to also treat non-convex tumour shapes, i.e. tumours wrapping around critical structures like the spine or the cochlear nerve. Using gantry-based devices with MLCs, it is also possible to dynamically compensate for organ motion by adapting the MLC shape [24, 30, 31, 36, 38, 67]. Tracking the tumour position can either be done in a similar fashion to the CyberKnife system, i.e. using room-mounted X-ray cameras like it is done in Mitsubishi’s RTRT system, or by using an MV imager [55] which is available for most gantry-based systems. On top of this, the manufacturers offer additional kV imaging, mounted orthogonally to the MV treatment tube, to be able to determine the true 3D position of the target. First experiments with this setup were done in [21]. Respiratory motion tracking with combined kV/MV imaging has been shown to be possible [64].

Fig. 2.9: Varian/BrainLAB’s Novalis Tx™ system1 (source: www.brainlab.com)

\(^2\) m3® is a trademark of Brainlab AG in Germany and the US.
2.4 Tomotherapy

A completely different approach to IMRT uses systems based on CT-scanners. These systems can deliver radiation in a coplanar fashion using an X-ray source. The technology is called tomotherapy, due to its similarity to tomography [27]. Serial tomotherapy describes the delivery of multiple fan beams with discrete couch position increments between each axial gantry arc, while in helical tomotherapy the gantry and couch motion are synchronised and happen simultaneously (i.e. the source describes a helical trajectory from the patient’s point of view) [20, 58]. Tomotherapy devices are manufactured by TomoTherapy, Inc. (the Hi-Art® system, see figure 2.11a) and Best nomos® (the nomosSTAT® system, see figure 2.11b). The Hi-Art system is a stand-alone machine based on helical tomotherapy and it also incorporates a CT scanner. The nomosSTAT system, on the other hand, is based on serial tomotherapy and is an add-on device to classical gantry-based treatment devices.

To date, respiratory motion compensation using tomotherapy machines is not clinically available. It is a topic under investigation, however, and recent works show that it is feasible to significantly improve plan delivery using motion compensation strategies [25, 26].

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2.5 The CyberHeart Project

A new application of robotic radiosurgery has been envisioned by Pankratov, Benetti, and Vivian in 2005 [37]. Their patent was subsequently acquired by Thomas J. Fogarty, M.D., who, together with Roderick A. Young, then founded the company CyberHeart, Inc., dedicated to developing the robotic ablation treatment for cardiac arrhythmia described in this patent. At the moment, the company is investigating the possibility of curing atrial fibrillation by means of radiation.

2.5.1 Medical Background

Atrial fibrillation (ICD-10 code I48), is the single most common manifestation of abnormal heart rhythms. It involves uncoordinated contraction of the muscles of the two upper chambers of the heart. These contractions are triggered by disorganised electrical impulses obscuring the normal excitation generated by the sinoatrial node. These impulses most frequently originate from the atria themselves or from the pulmonary veins. Atrial fibrillation by itself is mostly asymptomatic but results in an increased risk of stroke. Additionally, patients with chronic atrial fibrillation are often subject to cardiac insufficiency. Atrial fibrillation is very common in the general population: about 4.5 million people in the EU suffer from it and 25% of all people in the EU over 40 years old are expected to develop atrial fibrillation in their life [33].

Atrial fibrillation is, nowadays, usually treated with medication or by synchronised electrical cardioversion. If these methods are not available or have failed, RF ablation is used. The goal of RF ablation is to place lesions on the heart tissue from inside the atria or to remove parts of the muscle bundles around the end of the pulmonary veins. Major disadvantages of RF ablation are frequent side effects, like thromboembolism and stenosis of the pulmonary veins, and the long duration of the intervention. Even so, RF ablation is considered the gold standard in treating atrial fibrillation [1].
2.5.2 Technical Details

Planned as an extension of the CyberKnife system, the CyberHeart project endeavours to cure atrial fibrillation by placing ablation lines around the pulmonary veins to block electrical excitation emanating from these spots. This procedure is to be done on the beating heart using a modified version of the CyberKnife [49]. Feasibility studies and first pre-clinical trials have been done and show promising results [29, 50].

As a consequence, very precise localisation of the pulmonary veins and compensation of both respiratory and pulsatory motion is required. That the detection of the pulmonary veins using live 3D ultrasound actually is possible has been demonstrated [8, 9]. Furthermore, the application of algorithms developed with the goal of human respiratory motion prediction to pulsatory motion will be investigated in section 4.7.

Apart from this novel approach, there also is a limited number of patients who actually suffer from cardiac cancer [56] or tumours which move with pulsation [57]. Treating such lesions will also require detecting and compensating for cardiac motion.

References


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Compensating for Quasi-periodic Motion in Robotic Radiosurgery
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