Utilisation of portal imaging in positional control

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Introduction

Radiotherapy treatment is a sophisticated chain of technical events that relies substantially on the ability to locate the target volume within the patient with precision. Some of the major steps in the radiotherapy treatment chain are outlined below:

- Patient immobilisation.
- Treatment planning.
- Determination of tumour and normal tissues volumes.
- Simulation.
- Radiotherapy delivery.
- Treatment verification.

Accurate, reliable and appropriate images are needed to ensure that staging of disease extent, delineation of volumes of interest such as tumour bearing regions and identification of organs-at-risk (OAR), organisation of treatment planning, and verification for radiotherapy are optimal. This is especially important in three dimensional (3D) radiotherapy where conformal (CFRT) or intensity modulated (IMRT) techniques are being used. However there are numerous uncertainties that can be present within this chain of events of the patient's treatment pathway from the determination of treatment volumes to patient setup and during treatment delivery for a radical course of daily fractionated radiotherapy.

Radiotherapy Treatment and Delivery Associated Errors

The important sources of errors may be categorised and grouped in the following list and will be discussed later on.

- Patient group, equipment or protocol related errors
- Treatment preparation errors (systematic)
- Delivery related errors (random)
- Intra-fractional errors (physiological activity)

When we look more closely at the geometrical steps where uncertainties may compound positional errors in the design and delivery of radiotherapy, this can be illustrated by the following exemplars.

When the patient is computed tomography (CT) scanned for planning in the treatment position, skin tattoos are marked on the patient's skin and aligned with the CT room lasers. These lasers are then aligned with the CT room coordinates. This then represents the treatment set-up upon which subsequent radiotherapy is determined. However during radiotherapy delivery itself, the patient's set-up from the CT room needs correlation with the treatment room lasers. There may also be 3D positional changes between the skin marks and patient's bony anatomy as well as the position of the tumour relative to the patient's bony anatomy.

It is also important to measure and determine the magnitude of treatment errors, both systematic and random. One common and current method to determine the magnitude of treatment positional errors is portal imaging. This will also enable the reduction of positional errors. Portal imaging has been compared to simulation images but ideally should be correlated to digital reconstructed radiographs to enable verification of beam position and bony anatomy. It will be clear to any clinical practitioner that the pattern of errors will differ depending upon the type of tumour being treated and this is directly related to the location of the anatomical organ or region.

Planning Margins

Treatment margins are an important aspect of treatment planning. Determination of the margin needed is a careful consideration. Inadequate margins will result in lower local control of the tumour and impact on survival whereas too large a margin will result in excessive irradiation of normal tissues or organs leading to unacceptable rates of treatment related complications. There are various algorithms currently available for the determination of target and normal organ treatment margins that account for the influence of both systematic and random deviations. This will enable more reliable provision of treatment margins from the clinical target volumes (CTV) to planning target volumes (PTV).

There are many conceptual methods of margin provision and thus it is clear that there is a lack of consensus on the optimum method. Simulations of real patient data have been re-

ported to ascertain the impact of geometrical variations on dosimetry but these assessments are very tumour and site specific (Killoran et al 1997, Mageras et al 1996). One method designed to be generalisable utilises computation of the probability distribution and involves the analysis of each possible treatment preparation error to the dose distribution on the CTV generating dose population histograms (van Herk et al 2002). The resulting simplistic PTV margin recipe to cover the CTV for 90% of the patients with the 95% isodose can be outlined as follows:

$$\text{Margin} = 2.5 \Sigma + 1.64 \sqrt{(\sigma^2 + \psi^2)} - 1.64\psi$$

Where approximated $\psi \approx 3.2 \text{ mm}$

$$\text{PTV margin} = 2.5 \Sigma + 0.7 \sigma$$

Σ = standard deviation of all systematic errors combined quadratically

σ = standard deviation of all random errors combined quadratically

ψ = standard deviation (width) of penumbra (Gaussian)

The margin recipe for normal organs (McKenzie et al 2002) can be outlined as follows:

$$\text{OAR margin} = 1.3 \Sigma + 0.5 \sigma$$

Rationale for image guidance

Another important source of error is organ motion. New advances with on-line imaging can now provide improved image guidance. Advanced planning techniques such as IMRT permit the creation of highly conformal dose distributions. These planning techniques are based on a planning 'snap shot' of the tumour position at the time of the planning CT scan. The derived PTV based on this planning CT scan may or may not be representative of the average location of the tumour and certainly cannot account for the exact location of the target at the time of radiation. Currently our capacity to design such intricate and precise treatment plans exceeds our ability to reliably and accurately deliver them. Therefore the benefit of conformal and intensity-modulated radiotherapy techniques is still limited by uncertainties in both patient set-up and internal organ motion.

Even if treatment set-up is reliable, the patient is cooperative and he/she can be comfortably stabilised for a period of time, organ motion will occur due to respiration and internal physiological movement such as respiration, involuntary muscle contraction, filling and emptying of organs (stomach, bowel, bladder and rectum). These physiological movements can alter the relative 3D spatial position of the PTV and the adjacent OAR compared to the initial CT planning scan on subsequent days of a curative course of fractionated radiotherapy. This movement, if not accounted for in the treatment volume, may result in geographical miss with reduced local control of the tumour. Treatment margins are usually prescribed to avoid such geographical miss but large planning margins for target and localisation uncertainty negate the value of CFRT/IMRT techniques and increase the potential for late tissue damage particularly if the OAR are irradiated to a higher dose than anticipated by being displaced into the high

dose radiation region. This has implications for radiotherapy regimes of dose escalation.

It is clear that the uncertainty in daily tumour localisation precludes accurate delivery of radiation during a course of radical fractionated treatment delivered over many days. This is particularly pertinent in anatomical sites where internal organ motion is present and of substantial magnitude. These motion effects urgently need to be understood and handled realistically, particularly at soft tissue sites, before they undermine the further benefits expected from CFRT and IMRT, dose escalated regimes or more sophisticated strategies that are designed for biological boosting of disease.

Adequate definition of the 3D spatial position of the intended tumour volume is needed not only online on a daily basis but in real-time during radiotherapy in order to provide the accuracy and reliability that is currently lacking in modern radiotherapy. Online evaluation of the target position and 3D knowledge of the target motion may also permit appropriate reductions in the planning margins that are currently used in many anatomical sites with the benefit of reducing normal tissue morbidity. Herein lies the rationale for image guidance in radiotherapy.

Image Guided Strategies

The implications of internal organ motion are site specific and depend on the anatomical region in question for example treating breast and lung cancers will require knowledge of the respiratory cycle in the delivery of radiotherapy whereas radiation of the prostate will require knowledge of the surrounding pelvic organs and their physiological activity such as rectal and bladder filling and emptying. It is important to define the magnitude, distribution, pattern, and type of organ motion for each anatomical region and its impact on the tumour situated within that region. In some situations, organ deformation is also an important issue. This is particularly relevant for organs that fill or empty such as the lungs, stomach, bladder and rectum. In order for image guidance to be fully effective, 3D anatomical information is needed to enable adequate implementation of any image guided program. This task has now been made easier with the recent developments in treatment imaging.

One of the new innovations in on-line imaging include kilovoltage (kV) cone-beam imagers mounted on the LINAC gantry permitting kV radiography that may provide improved superior bony identification compared to EPI megavoltage identification (Jaffray et al 2002). Importantly, it can also provide cross-sectional imaging for online 3D verification and online fluoroscopy for real-time assessment of target and organ motion for dynamic tracking and gating similar to robotic LINACs. Online 3D target motion knowledge may allow treatment margin reductions with benefits of reducing normal tissue morbidity. Cone beam imaging may also be correlated with functional imaging for response evaluations for selective management. Some examples using this technology will be discussed later on.

Radiotherapy in the thorax

This is a site that is plagued by known physiological motion that is significant in its magnitude. Tumours located in the thorax such as lung and breast cancers can be displaced

by both respiratory and cardiac motion. Respiratory motion can be monitored or made predictive in order to develop methods to sensibly deal with this motion. There are several techniques available to deal with reducing the effect of respiratory motion such as central abdominal compression, active breathing control (ABC) device or the use of external thorax infra-red marker systems for monitoring respiratory cycles.

The use of the active breathing control (ABC) device allows for voluntary control of the respiratory cycle by the patient. Using the ABC device, gating treatment methods can be introduced by asking the patient to breath hold for the radiotherapy treatment in lung and breast cancers as well as Hodgkin's disease (Wong et al 1999, Stromberg et al 2000). The surface of the thorax may also allow the use of surface guided active monitoring of the respiratory cycle or the use of externally placed infra-red marker systems that can measure the breathing cycle and amplitude of oscillation. Recent studies suggest that whilst values may vary substantially between different patients, there is consistency and stability for the individual patient within each daily treatment or during a course of treatment. These techniques can lead to programs of free-breathing phase gated radiotherapy (Korremans et al 2003).

Bladder Radiotherapy

The position of pelvic tumours can be affected by movement of the bowel, filling and emptying of the bladder and rectum. Bladder cancer is a good example. Significant variation in physiological activity with bladder filling/emptying as well as bladder motion has been reported (Turner et al 1997, Meijer et al 2003). In a study of 30 patients imaged sequentially during a curative course of radiotherapy, a change in bladder area of up to 55% was recorded despite a consistent protocol of bladder emptying prior to scanning (Turner et al 1997). In addition, 60% of cases demonstrated bladder wall movement of greater than 15 mm relative to the 95% prescribed isodose line. This data illustrates that significant movement can occur during radiotherapy and simply increasing the treatment margin to encompass this variation is not an optimum solution.

There are adaptive and predictive methods to enable 3D changes in target volume to be tailored to the individual patient. Adaptive radiotherapy methodology utilises initial assessment of daily bladder treatment volumes to select a smaller range of treatment plans most likely to represent the majority of daily shapes in each patient. Using on-line daily assessment the best fit bladder plan is selected from an acceptable range of bladder plans for use each day. Predictive radiotherapy methodology necessitates the evaluation of the individual patient's pattern of volume enlargement and deformity. This can be performed using cine magnetic resonance imaging. The extent of change depends on several factors that are both patient and tumour dependent. Using time dependent patterns of individual patient's bladder deformity, treatment volumes may be predicted on a daily basis. Both these methods are not mutually exclusive and each method has its respective pros and cons. However, in order to implement either technology, 3D methods of on-line assessment are needed to provide the necessary 3D data.

Prostate Radiotherapy

Radiotherapy is an important form of curative treatment for both early and locally advanced prostate cancer. Prostate radiotherapy is another good example where prostate organ motion and patient set-up error are important uncertainties that need to be addressed in the external beam irradiation of the prostate gland during a fractionated course of radiotherapy. This is particularly pertinent as many dose escalated programs using IMRT have been utilised in this disease.

It is well known that the anatomical position of the prostate gland and seminal vesicles can be affected by the physiological movements of the surrounding pelvic organs such as the rectum and bladder. Studies have assessed prostate movement using repeated computed tomography (CT) scans over the course of radiotherapy (Ten Haken et al 1991, van Herk et al 1995, Beard et al 1998, Dawson et al 1998, Zelefsky et al 1999). Some investigators have used radiographic films with or with CT and aided by implanted radio-opaque prostatic markers (Balter et al 1995, Crook et al 1995, Vigneault et al 1997). From these reports, the mean inter-fraction displacement of the prostate gland has been reported to range between 3 to 7 mm with the majority of movement in the antero-posterior axis followed by the superior-inferior axis. More recently, potential intra-fraction movement in prostate cancer patients has been assessed using cine MR (Padhani et al 1999, Huang et al 2002, Mah et al 2002, Nederveen et al 2002). The median prostate displacement was reported to be in the anterior direction of 4.2 mm and in 16% of patients, the movement was greater than 5 mm (Padhani et al 1999). More recent studies have reported that the average intra-fraction displacement is smaller than 4 mm. For the individual patient, prostate positional changes may be substantially larger than the reported average displacement for the population under study. These changes in tumour position for the individual need to be accounted for with larger treatment margins which can be avoided if real-time tracking and gating of the treatment beam is available.

Various monitoring strategies both off-line and online with adaptive or real-time manipulation of the treatment delivery have been utilised. Immobilisation of the rectum using rectal balloon have been used to more reliably reduce the interaction of the rectal displacement of the prostate (Wachter 2001). Daily relocation of the target prior to treatment has been used using a stereo-coordinated ultrasound device linked to the treatment bed (Lattanzi et al 1999, Lattanzi et al 2000, Chandra et al 2003). There is some early work performed to use implanted markers for tracking in prostate cancer in Japan (Shimizu et al 2000, Kitamura 2002). This system requires specialized installation of stereotactically orientated image intensifiers housed within the floor and ceiling of the treatment delivery room to spatially coordinate the location of implanted markers. One potential advantage of using a cone beam system such as that from the Elekta Synergy or Varian On-Board Imager is that it will not require such specialised bunker room installation or increased room space as it is mounted on the linear accelerator. In this manner, this technology can be more easily transported to radiotherapy departments world-wide.

Dose escalation hypofractionated regimes using IMRT are being studied for prostate cancer patients at both the Christie and Royal Marsden Hospitals in anticipation of improved cu-

re rates and reduced morbidity by exploiting the low γ ratio reported in prostate cancer. Reliable accurate targeting of the prostate gland is thus necessary to improved localisation and reduce radiation dose to the adjacent rectum and bladder. The ability to track the prostate PTV in real time during treatment delivery and provide beam gating will be an important development to ensure that the potential of dose escalation with CFRT or IMRT techniques is realised. This technique will also address the essential question of treatment verification and allow quality assurance of the treatment program.

Summary

Treatment verification is crucial for precision radiotherapy irrespective of the treatment techniques being used. Current methods of electronic portal imaging has provided quality assured standards in modern radiotherapy. However there are now significant advances in on-line 3D imaging such as kv imagers and cone beam CT acquisition. There is an opportunity to obtain 3-D images with soft-tissue definition at all anatomical sites treated with external beam radiation therapy at acceptably low radiation doses. Image quality will be dependent on tumour site and dose delivered. There is much on-going work in optimizing image capture using this new technology. This technology has the potential for optimising generic population margins, customising and adapting treatments for individual patients, and accurate verification of complex treatment delivery. This technology may revolutionise current quality assurance programs and permit the development of new protocols for adaptive, predictive, gated or tracking in radiotherapy.

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