INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **51** (2006) R403–R425 doi:10.1088/0031-9155/51/13/R23

REVIEW

Motion effects in (intensity modulated) radiation therapy: a review

S Webb

Joint Department of Physics, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, UK

Received 1 December 2005, in final form 23 March 2006
Published 20 June 2006
Online at stacks.iop.org/PMB/51/R403

Abstract

During a course of fractionated radiation therapy and between the fractions the tissues of the human body may move relative to some reference location in which the radiation therapy was planned. This has been known for over a century and simple 'coping mechanisms' (margins) have been used to approximately compensate. Since the introduction of highly accurate conformal radiation therapy and intensity-modulated radiation therapy (IMRT) attention has focused strongly in the last few years on understanding and compensating more appropriately for these motions. Thus, unlike most of the reviews in this special 50th anniversary issue which look back over decades of development, this one looks back at most within just the past decade and reviews the current situation. There is still much more work to be done and many of the techniques reviewed are themselves not yet implemented widely in the clinic.

1. Introduction

The use of intensity-modulated radiation therapy (IMRT) to sculpt the high-dose region around the target and to spare organs at risk is now well established and many theoretical, experimental and clinical studies have been published (see reviews by Webb (1993, 1997, 2000, 2004), Palta and Mackie (2003)). No-one doubts that better dose distributions can be formed through IMRT but the clinical efficacy is yet to be uncontroversially demonstrated. Meanwhile, attention has moved on to addressing the question of understanding the motion of organs and tumours and compensating for this at treatment. This *advance* is really a *return* to re-state that the most important aspect of radiation therapy is locating the target and ensuring that it is where it is supposed to be at the time of treatment. Identifying the target location at planning depends on multimodality imaging and is not the subject of this review. This review concerns ensuring that the target is geometrically linked correctly to the beams throughout irradiation.

Whilst this topic is newer than the development of IMRT, there is nevertheless a large literature and this review attempts to distil the essence of this and to concentrate mostly on the more recent developments. A very lengthy review up to the summer of 2004 already appeared in Webb (2004), although here that material is again distilled for completeness and updated. This paper is an 'odd man out' in this anniversary issue. Whereas others can take a long retrospective view, this is not possible for this topic which is extremely new. Indeed very little has yet reached clinical practice.

There is some circularity in this area. Logically, the first task would be to establish the magnitude of the motion effects and secondly to devise ways to compensate for them. However, some of the measurements have only become possible following intervention strategies that were devised more with compensation for motion in mind. For example the implantation of radio-opaque markers in organs, continuously viewed by fluoroscopic x-rays, clearly suggests an approach to feeding back the knowledge of motion for compensation. Yet equally, in turn, it generates further knowledge of the scale of the problem.

2. PTV or CTV conformality

There is nothing new about organ motion. Treatment planners have always known that organs move and have compensated for this by expanding the clinical target volume (CTV) by a margin to form the planning target volume (PTV) to which treatment is conformed. By adequately irradiating the PTV, in which the CTV moves around from fraction to fraction (interfraction motion) and during fractions (intrafraction motion), the irradiation of the tumour is assured. For some time it was thought that this construct would fail for IMRT but Bortfeld *et al* (2002b) showed that, provided each fraction is dephased relative to the others (which will occur naturally), the exact same concept holds for IMRT. So, if one is content with doing no better than in the past, one can stop at this point and stay with margins although even this does not cope with systematic error. Recently there have been many papers explaining formulae for such margin generation (e.g. Van Herk (2004)).

Conversely, this is too unchallenging a goal. We want to irradiate only the CTV, since that is where the disease resides. To do this we need to know the inter- and intra-fraction motion of the CTV and then alter the irradiation technique to cope by either (i) natural or assisted breath-hold to gate the treatment to a small range of motion of the CTV, or (ii) track the motion and track the collimation (e.g. the MLC leaves) proportionately. The first has a lower than 100% duty cycle; the second has a 100% duty cycle.

Not everyone agrees that all patients need assessment and compensation for motion and an interesting debate by Herman *et al* (2003) reviews the arguments on each side.

Most published studies could be catalogued (i) by inter- versus intra-fraction motion, (ii) by method of determining motion, (iii) by method of intervening to compensate for motion and (iv) by organ studied. However, given the many varied and disconnected approaches to studying organ motion, there are many ways the studies and papers could be organized. I have chosen just one way as follows.

3. General observations

The most comprehensive publication on organ motion and its management by Langen and Jones (2001) collated tables of studies for liver, diaphragm, kidneys, pancreas, lung, bladder, rectum and prostate from 66 studies. The deduction of generalities was hampered by many different experimental conditions and readers should refer to these tables for details.

4. Optical imaging for motion correction

Tomé *et al* (2000, 2001) used a biteplate attached to the patient's maxillary dentition and attached to which was an array of passive infrared markers viewed externally. As the patient moved, the information was fed back to a compensating stereotactic delivery system. The BrainLab ExacTrac optical-navigation-and-guidance system has been used by Alheit *et al* (2000), Hagekyriakou *et al* (2000), Verellen *et al* (2000) and Kim *et al* (2004) for imaging external infrared markers, said to be correlated to motion of the prostate and head-and-neck tumours. Wagman *et al* (2001) used the Varian real-time position-monitor (RPM) passive-infrared-marker system to both acquire gated CT data and to gate treatment for the liver. George *et al* (2003) used the RPM system to image the breast and showed that the CTV dose inhomogeneity increased with amplitude of respiratory motion. This study also showed that, averaging over a full course of fractions, the motion-adjusted distributions well matched the planned distributions for the PTV. Skin-mounted infrared markers have been used by Lyatskaya *et al* (2002) to monitor breast movement. Optical stereophotogrammetry has been used by Macpherson *et al* (2002). Moore and Graham (2000) also created interference patterns of structured light and an optical stereophotogrammetry device to create a computer image of the patient surface which could be 'docked' to a reference shell to indicate appropriate translations to accommodate interfraction motion.

5. X-ray imaging for motion assessment and correction

The most common, though invasive, way to measure motion is to implant fiducial markers in an organ and observe their motion with fluoroscopy. Murphy *et al* (2003) built up a picture of intrafraction tumour movement this way for 250 cranial, 23 spinal, 9 lung and 3 pancreas patients. Gradual intrafraction drifts were observed; mean data are of no practical interest and individual motion patterns show both rhythmic and irregular (outlier) unpredictable motions.

5.1. Prostate

Balter *et al* (2000) showed that, for the prostate, craniocaudal motion was largest and was much lower for supine setup than prone setup and even lower if a false table top allowed the pelvis to fall posteriorly. Often-quoted studies are those of Kitamura *et al* (2002) who monitored 10 patients each 5 times with fluoroscopic imaging of gold markers at 30 Hz to create pictorial trajectories of the targets with conclusions in agreement with those of Balter *et al* (2000). Nederveen *et al* (2002) used portal imaging to assess prostate marker motion during a fraction every 0.4 s. Ten patients with 251 fractions were studied. Mean motions were small but outlier maximum motions were of the order 9 mm. Spitters-Post *et al* (2002) and Visser *et al* (2002) showed prostate marker movement relative to bony landmarks.

Highlighting one specific study, Aubrey *et al* (2004) have implanted two or three fiducial markers in the prostates of 18 patients and imaged them with CT (to provide baseline position information) and subsequently with online portal imaging. Data were acquired on the translation of the centre of mass and on the rotation of the prostate. Where possible the patients were instructed to achieve a full bladder and empty rectum to try to achieve as reproducible a position as possible. Interfraction variations were assessed from the data at each fraction compared with baseline and intrafraction variations from before-and-after therapy imaging at any specific fraction. Note this is *not* the same as measuring the prostate position during irradiation. (This is more grammatically correct intrafraction motion measurement and the other use of the term is somewhat confusing.)

The overall standard deviation of intrafraction translations was 0.8 mm L-R, 1.1 mm S-I and 1.6 mm A-P. Graphs of the distributions showed that, whilst mean intrafraction displacements were almost identically zero, the distributions were quite broad with outliers greater than 5 mm. The authors commented that the intrafraction movie loops of Padhani *et al* (1999) showed large motions but over short times, completely different data to that acquired in this study.

The standard deviation of interfraction rotations was 8.0° about the L-R axis, 3.6° S-I and 2.9° A-P. Again, mean rotations over the population were close to zero but large outliers arose. The standard deviation of intrafraction rotations was 5.8° about the L-R axis, 3.8° S-I and 2.0° A-P. Again mean rotations over the population were close to zero but large outliers arose. They deduced that intrafraction rotation was less important than interfraction rotation and these latter were larger than reported in other previous studies.

5.2. Lung

Shimizu *et al* (2000, 2001) have used the same system as Kitamura *et al* (2002) to record the movement of implanted lung-tumour markers at 30 Hz showing that, with free breathing, markers moved up to 16 mm. The knowledge was used to gate an accelerator and reduce this excursion during irradiation to 5 mm. Seppenwoolde *et al* (2001, 2002) similarly plotted lung-tumour marker trajectories demonstrating that dwell-time was greater at maximum exhalation than inspiration and, again, gating an accelerator with the data (see section 8.3).

5.3. Relation between internal marker motion and external marker motion

Kini *et al* (2001) studied 150 fluoroscopy movies for 6 patients for whom there was also simultaneous monitoring of the chest wall through camera-based infrared markers. The two motions were linked with a phase shift in time and then, using this relationship, the internal motion, predicted from the external motion, was shown to agree to within 3 mm with the actual internal motion. Vedam *et al* (2001, 2003a, 2003b) used a similar correlation to predict the diaphragm motion from a measurement of external markers using the Varian RPM system at 30 Hz.

Gierga *et al* (2005) studied the relationship between the motions of internal (clip) markers implanted in liver tumours and the motion of surface-mounted infrared markers. Respiratory gating on external markers relies on a good correlation between these two motions. Such a correlation was generally observed but there was often a very large ratio between the excursion of the tumour marker and the excursion of an external marker, this ratio depending on patient and on the locations of the markers. Hence one cannot simply assume that the external excursion equals the internal excursion. Also, worryingly, the location of an internal marker could have as much as 9 mm variation for the same location of external marker.

This topic is considered in section 9 in relation to the Cyberknife.

5.4. Mathematics of breathing

Patients breath asymmetrically and a much-used representation, determined from x-ray fluoroscopy, is that from Lujan *et al* (2003), a form of which is

$$z(t) = z_0 + b\cos^{2n}(\pi t/\tau + \pi/2)$$

for motion in a z-direction where t = time, z_0 = exhale position, b = peak-to-peak amplitude, τ = breathing period and $2n$ = shape parameter. As $2n$ increases, more time is spent at end

expiration. A value of $2n = 6$ has often been used but extensive data fitting by George *et al* (2005) showed $2n = 4$ modelled better but even considered cos to be adequate. If a static dose distribution is convolved with such a function it gives an approximate indication of the motion degradation. Sadly, real breathing can be more erratic with changes in amplitude, period and shape and occasional wild excursions during the breathing cycle (Seppenwoolde *et al* 2002, Nøttrup *et al* 2005). This must be remembered when reading studies and motion-correction techniques based on this equation.

5.4.1. Intrafraction breathing margins. Engelsman *et al* (2005) have also demonstrated that patients' breathing often changes throughout the period of irradiation in both amplitude, baseline shift and shape. They took fluoroscopic data from Hokkaido University and, for 40 patients, plotted the probability density function (p.d.f.) of breathing. (Similar p.d.f. data were generated by Díez *et al* (2004).) Sometimes this could be fitted by the Lujan equation but in 90% of cases the data could be as well fitted with a Gaussian function specified by a median peak-to-peak amplitude and a standard deviation which was 0.4 times this median amplitude. They then modelled the breathing degradation of a 1D dose profile by convolving the p.d.f. with the 1D profile and showed the extra margin that was required to restore the target coverage to that in the unbreathing situation, in terms of either the median amplitude or the standard deviation of the p.d.f. The extra margin was not linear with median amplitude and standard deviation. Figure 1 in the review shows the increasing gradient of the curve of required extra displacement versus these parameters. Alternatively, if breathing-control manoeuvres reduce the amplitude of breathing, the data from the study showed the reduction in margin which can be permitted under ideal conditions. As far as intrafraction breathing is concerned it was concluded that, being random, the error indicated by this standard deviation could be added in quadrature to other random errors (for patient positioning etc) to indicate the overall margin to convert from CTV to PTV. Results were shown to be in line with predictions of formulae from Van Herk (2004). Also for patients with a peak-to-peak amplitude of less than 10 mm, control of breathing only allows a small reduction in safety margins.

6. Ultrasound location of tumours

The main commercial apparatus for ultrasound location of tumours is the NOMOS beam acquisition and targeting device (the BAT) which has been used mostly to give a pre-treatment interfraction measurement of the prostate. The contour of the prostate is then extracted (not always easily) and correlated with the contour from the treatment-planning CT slice. Misregistration then gives the docking translations required. Clearly this can only be correct for rigid-body shifts. Sometimes one reads that it can make intrafraction measurements (Huang *et al* 2002) but this is a misnomer and refers to a comparison of before- and after-treatment fraction. There have been many published studies including those by Lattanzi *et al* (2000), Beyer *et al* (2000), Willoughby *et al* (2000), Trichter and Ennis (2001), Falco *et al* (2001), Chandra *et al* (2001, 2003), Morr *et al* (2000, 2002), Héon *et al* (2002) and Little *et al* (2003). Most of these studies reported on large numbers of patients and gave the mean and standard deviation of motion in three orthogonal coordinate directions. However, of much more importance is the general observation of outliers, occasions on which the target was grossly mispositioned. There is some discussion of operator training, interoperator comparisons and operator self-comparison. Interestingly, Van den Heuvel *et al* (2003) and Langen *et al* (2003) find the BAT of no use for predicting the motion as assessed from implanted markers.

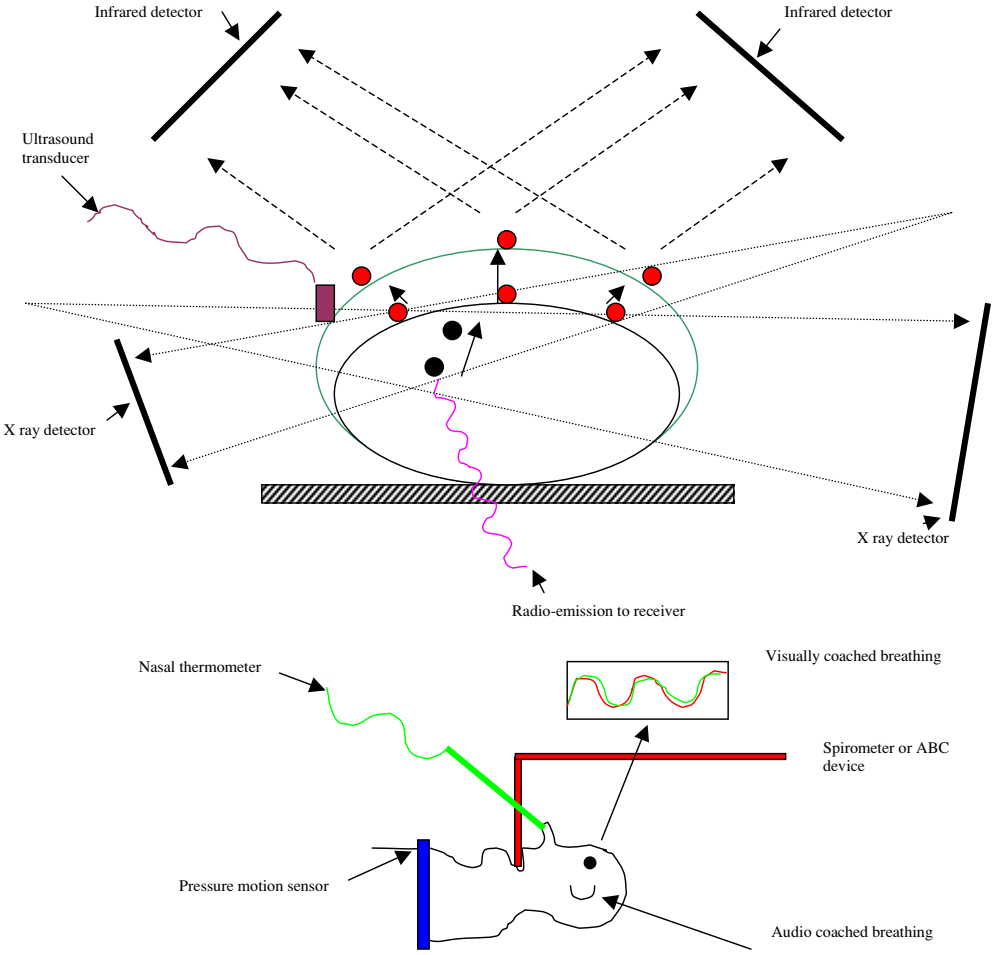

Figure 1. Cartoon schematic showing the several ways to measure the motion of a tumour (not all at once as drawn!). Note the tumour (black circle in upper drawing) motion is drawn in a different direction to the patient surface motion (black to green contour) to emphasize the need to correlate internal and external motion if motion tracking is to be based on the use of external markers. There could also be phase differences. Tumour motion can be measured directly by x-rays, ultrasound and radio-emissions and indirectly by surface infrared markers (red circles). Other gating techniques could rely on measurements of nasal temperature, abdominal pressure, spirometry, ABC or visual or audio coaching.

Others have built their own equipment. Bouchet *et al* (2000) attached light-emitting diodes to an ultrasound probe to record its in-room location for registration with 3D data. Sawada *et al* (2002, 2004) have a CT scanner, ultrasound scanner and linac together in the same room. At CT scanning, ultrasound measurements are also made and then, using further ultrasound data recorded during treatment and correlated to the first set, the linac is gated if the target drifts away from the expected location.

Artignan *et al* (2002, 2004) showed that the pressure applied by the ultrasound probe actually displaced the prostate by 3 mm for every 1 cm of applied 'pressure'. Conversely, using MR images, McNeeley *et al* (2003) disputed this, finding only 1 mm prostate movement due to transducer pressure.

7. Magnetic monitoring of position

Seiler *et al* (2000) and Muench *et al* (2001) have implanted a wire-coupled position-sensitive sensor into tumours and tracked its motion using an external magnetic field. The accuracy was reported to be of the order 1–2 mm. Balter *et al* (2003, 2005) have described a wireless localization system. One or more wireless transponders or beacons, glass encapsulated, are implanted in the organ whose motion is to be tracked. A magnetic source and receiver coil array then determines the transponder positions provided they are in a field of view of 14 by 14 cm^2 and up to 27 cm away from the array. In turn, a set of infrared cameras in the room views the array and the combination of determining the position of the array w.r.t. the isocentre and the position of the beacons w.r.t. the array gives the position of the beacons w.r.t. the isocentre. The system is known as Calypso. Experiments showed that the beacons can be tracked with submillimetre accuracy both in air and also in saline solution simulating the electrical conductivity of tissue. Moreover it has been demonstrated that there is no crosstalk between the transponders. The advantages over a corresponding wired system are obvious and, since the system makes no use of external x-radiation, there are also advantages claimed over the use of implanted gold-seed markers.

8. Gating

Gating can, in principle, ensure that both the target is in the correct irradiation position and also that the normal tissues are excluded from too much irradiation. The motion is tracked by some signal that then instructs the accelerator to irradiate only when the target is in a limited range of locations for which the planning has been performed. By definition the duty cycle is less than unity and indeed, if the position were too tightly specified, would be close to zero and impractical. Thus gating is a 'coping strategy'.

8.1. Gating irradiation of oscillating phantoms

Kubo and Wang (2000) irradiated a static phantom. Then they irradiated the phantom on an oscillating stage and showed degradation of the dose distribution. Finally they gated the irradiation using pulses from a spirometer characterizing a real patient's breathing. This third dose distribution was close to that for the static irradiation. This study importantly showed that the characteristics of the accelerator did not change with gating and also that this equivalence was independent of energy, doserate and direction of motion gating. Hugo *et al* (2001, 2002) did similarly with infrared photogrammetry gating. See also section 12.4.2. Dietrich *et al* (2005) showed by experiment with moving phantoms and also by simulation that use of a small (3 mm) gating window did not significantly disturb the dose distribution from its static form and the increased treatment time was acceptable. With these phantom irradiation gating experiments in mind we proceed to consider clinical implementation.

8.2. Gating based on optical measurement of surface markers

Solberg (2000) and Kini *et al* (2000) have gated therapy using the information from infrared surface markers. Ramsey *et al* (2000) have gated lung therapy and Vedam *et al* (2001) specifically showed that gating on exhale is more reproducible. Keall *et al* (2002) have proposed 4D IMRT in which respiratory gating accommodates movement in the thorax. Nelson *et al* (2005) have gated on voluntary deep-inspiration breath-hold using a patient-viewable optical-marker-generated breathing trace. Berbeco *et al* (2005c) showed that two

ways of gating based on external surrogate tumour markers did not greatly reduce residual tumour motion during irradiation. Berbeco *et al* (2005b) instead used an EPID in cine mode.

8.3. Gating based on x-ray fluoroscopic markers

Shirato *et al* (2000a, 2000b, 2004a) used four sets of diagnostic x-ray television systems in the treatment room to track the location of a 2 mm gold marker in prostate, lung and liver at 30 Hz. The treatment and diagnostic x-rays were never on together, arranged through appropriate pulsing. The diagnostic procedure contributed 1% extra dose. The image data were used to gate the linac, reducing the range of travel of tumour markers typically from some 3.8 cm to 5 mm. It was claimed this is more accurate than tracking surface markers which may or may not correlate with deep-seated marker seeds and better than magnetic monitoring which is invasive. Sharp *et al* (2003) claimed no need to use predictive techniques (see section 12.5). Shirato *et al* (2004b) later pointed out that the technique of using continuous fluoroscopy can lead to excessive unwanted dose and this is a motivation behind the quest for non-irradiation techniques.

8.4. Gating based on respiration monitor

Jiang and Doppke (2001) used a spirometer to gate CT acquisition, reconstructing data at three phases of breathing for breast planning, concluding breathing was not a major problem. Giraud *et al* (2000) also used a spirometer to gate CT scans and proposed gating therapy correspondingly. Zhang *et al* (2003) showed the long term drift in spirometer monitoring and developed a calibration technique to overcome this. Van Herk *et al* (2002) used a nasal thermometer to measure the breathing phase and gate CT data.

Butler *et al* (2004) conducted a study to determine whether more normal lung tissue was excluded from high dose when treating a lung tumour if the radiation were gated. They studied gating on deep-inspiration breath-hold (DIBH; generally 60% of vital capacity), or on 0% (full expiration) and 100% (full inspiration) of tidal volume. This study created treatment plans on the CT datasets at these breathing phases and analysed the dosimetry using dose–mass histograms (DMH) rather than dose–volume histograms. This choice was made because a DMH more realistically represents the number of tissue cells damaged (Nioutsikou *et al* 2005). Comparisons were made with plans created using free-breathing CT datasets. It was found that gating at each of these positions reduced the dose to normal lung. A key parameter studied was M20, being the mass of lung tissue receiving at least 20 Gy. Ratios of this parameter for gated therapy compared with free-breathing therapy were created and found to always be less than unity. However, for some patients, the ratio was very close to unity, indicating little benefit from gating. Also there was no correlation between the gating benefit and the tumour type or location meaning that, ahead of time, patients could not be pre-selected for gating on any classification basis. Individual studies had to be performed.

8.5. Held breath self gating

Some studies have been based on asking a patient to hold their breath for a deep inspiration breath-hold (DIBH) and the irradiation takes place only during this period. Mah *et al* (2000) showed this locked the tumour position to the corresponding planning position to better than 2 mm for a large number of patients. Kim *et al* (2001) experimented with four different parts of the breathing cycle for breath-hold. Mageras (2004) pointed out that 60% of patients at MSKCC cannot comply with DIBH. Barnes *et al* (2001) presented an extraordinary range of

breath-hold periods up to 52 s and Della Biancia *et al* (2003) showed improved normal lung sparing at end inspiration compared with end expiration.

8.6. Gating based on density changes

Berbeco *et al* (2005a) have proposed that the fluoroscopically observed change in density of lung can be used to gate to specific breathing phases.

8.7. 4D cone-beam CT/kVCT

Cone-beam kVCT has recently been established as an available tool on a radiotherapy linac, the concept being that a kVCT scan recorded just before treatment can be compared with the planning CT scan and adjustments made to compensate for mispositioning. Generally, however, a kVCT scan takes typically tens of seconds to record and again tens of seconds to reconstruct (although reconstruction can take place during the scanning period). Since this scanning time is considerably longer than the breathing period the resulting kVCT scans would be blurred if no further action were taken. Sonke *et al* (2005) have developed a method to extract the breathing signal from each projection based on a measurement of the projected position of the diaphragm. Then the projection data were re-sorted *a-posteriori* into just eight phases of the breathing cycle and these subsets of data were used to make eight kVCT scans which, viewed as a set, constitute a 4D kVCT reconstruction. Of course the signal-to-noise ratio will deteriorate as a result of the fact that fewer projections now comprise each reconstruction. However, it was found that signal-to-noise ratio did not deteriorate to the point that the organs were unable to be identified. Careful experiments were made with a phantom to show that the phase-re-sorted kVCT reconstructions did correspond well with the equivalent kVCT reconstructions of static phantoms at the same breathing phase.

9. Robotic feedback

The Accuray Cyberknife is a robotically held linear accelerator capable of pointing in many non-coplanar directions. Thus it is the ultimate in IMRT geometric capability although presently, equipped with a circular small-field collimator, is too inefficient for most IMRT. Its strength is its linked motion-compensation system. Infrared markers on the patient's skin are tracked in real time by a camera system. Every 10 s x-ray images are taken of implanted markers. An algorithm links the two measurements such that a continuous measurement of the external markers is converted into a pseudo-continuous measurement of the internal markers. This latter can be fed back to the robot so that it can 'track the breathing organs' (Schweikard and Adler 2000, Schweikard *et al* 2004) (see also section 5.3).

10. Active breathing control

Active breathing control was invented by Wong (2003) who modified a ventilator to enable the patient to be coached to determine their tolerance to breath-hold. Once this is established, an option is for the patient to view their breathing trace and the air is cut off for a fixed period during which the target is immobilized and the irradiation takes place. Stromberg *et al* (2000) showed that, with breathing controlled at deep inspiration (DI) when irradiating lung tumours, the dose–mass histogram of normal lung was reduced significantly with use of the ABC device. Similar results were recorded by Wilson *et al* (2001). Aznar *et al* (2000), Remouchamps *et al* (2002, 2003) and Sixel *et al* (2001) showed that DI improved the sparing of heart in

left-breast radiotherapy. The technique is also in use at the Royal Marsden NHS Foundation Trust (Donovan *et al* 2002, 2003, McNair *et al* 2003, Christian *et al* 2003). Dawson *et al* (2000) used the device to immobilize the liver.

11. Calculating the effect of tissue motion

11.1. Including the motion concept in treatment planning

Li and Xing (2000a, 2000b) proposed a method to incorporate the expected motion into planning. If $D_f(n)$ is the dose to voxel n without taking account of motion and $P(n, n')$ is the probability of finding voxel n at n' then the dose really received by n is

$$D(n) = \sum_{n'} P(n, n') D_f(n)$$

and so planning should minimize the function

$$(1/N) \sum_{n=1}^{N} r_s [D(n) - D_0(n)]^2$$

where r_s is the importance factor for structure s and N is the total number of dose calculation points. Minimizing this function minimizes the difference between the prescription and the motion-smoothed dose distribution. Xing *et al* (2000) showed that not doing this led to degraded plans by comparison. An alternative proposed by Loof *et al* (2001) incorporated the motion into the dose kernel used in inverse planning. Unkelbach and Oelfke (2003, 2004a, 2004b, 2005) have also developed a planning method that accounts for the probabilistic dwelltime of a tumour evaluated from multiple CT scans.

11.2. Use of multiple CT datasets and adaptive IMRT

Several workers (e.g. Xu *et al* (2000), Bignardi *et al* (2000), Plasswilm *et al* (2002), Hoogeman *et al* (2003) and Large *et al* (2001)) have shown that, if the plan created from a CT dataset on day 1 were applied to CT datasets on subsequent days/weeks, the dose distribution would be inappropriate. These detailed studies quantitated the errors and pointed to the need to correct for inter-fraction variations in tissue geometry. Schaly *et al* (2004) actually tracked individual voxels using sequential CT datasets to create composite dose distributions correctly averaged over the fractions.

11.3. Composite target volumes

McShan *et al* (2001, 2002) and Fraass *et al* (2002) have developed the multiple instance geometry approximation (MIGA) in which two or more instances of geometry are recorded and the plan optimized for all instances concurrently. The plan is then worse than the 'no motion' plan but better than this latter convolved with motion. Martinez *et al* (2001) have used multiple CT scans in week 1 to tailor the PTV margin with confidence-limited anisotropic margins from CTV instead of fixed margins. Pavel *et al* (2001) and Mechalakos *et al* (2002) also studied the change in target geometry over the course of radiotherapy fractions.

11.4. Multiple CT scans and altered inverse planning

Bortfeld *et al* (2002c) determined the exact fraction number at which intervention should take place when daily measurements of target location were available in order to correct for the

systematic variation separately from the random effects. Typically the answer was about 4. Wu *et al* (2002) conversely computed the summed dose to the *n*th fraction and then re-optimized the $(n + 1)$th fraction accordingly.

11.5. Daily repositioning

X-ray CT in the treatment room allows the most direct way to reposition a patient each day correctly as their planning CT scan (Kuriyama *et al* 2003, Paskalev *et al* 2003, 2004, Dong *et al* 2004). Cone-beam kilovoltage CT is an alternative method to daily x-ray CT not covered in detail in this review.

Court *et al* (2005) have devised a method to adjust the MLC shapes on a daily basis using CT data acquired ahead of each treatment fraction. These data are compared with the planning CT data and the MLC shapes are adjusted to (i) account for global rigid body translations in the S-I direction and (ii) account for actual shape change of prostate and seminal vesicles due to daily change in rectum and bladder status. They showed that, provided the MLC shapes are so adjusted, the dosimetry to the PTV and OARs is considerably more faithful to the treatment plan than if simply global couch position adjustments had been made. It is this latter method which is the default use of pre-treatment kVCT data. The main improvement comes from the consideration of the daily volume changes of targets and organs at risks.

12. Intrafraction motion modelling

12.1. 4D CT

Van Sörnsen de Koste *et al* (2003) created three fast and three slow CT scans for each lung patient from which they deduced the optimum CTV as the envelope of the CTVs from each of these six. They found that if the CTV from the slow breathing scan were expanded by 5 mm symmetrically to form a PTV this PTV was close to that envelope. Conversely CTVs from the individual fast scans were too small. Allen *et al* (2004) also showed the relationship between CTVs determined from free breathing scans and end-tidal scans. Keall (2004) and Keall *et al* (2004b) gated a CT scanner with the signal from the RPM infrared system to create CT scans at different phases of the breathing cycle. This is generally referred to as 4D CT. Mageras (2001) and Mageras and Yorke (2004) used respiratory gating to create CT datasets at 8–10 phases of the breathing cycle and show movies of the breathing patient. Frazier *et al* (2000, 2004) gated CT using the ABC device to create scans of the breast at normal inspiration and normal expiration. These were used to show that dose distributions were fairly insensitive to breast motion during normal respiration.

12.2. Single fraction delivery

It has now been well established that, if intensity-modulated beams computed on a static CT scan are applied to a moving phantom or patient, the dose distribution will be severely degraded (Holmberg *et al* 2000, Kung *et al* 2000, Zygmanski *et al* 2001, Ramsey *et al* 2001). Several authors have shown this effect by delivering modulated fields to a phantom on a moving platform (Sohn *et al* 2001) showing the dose distribution differed significantly from the effects of convolving a static dose distribution with a motion kernel. This is entirely understandable because convolution will only approximately reproduce the effects of motion if the average is taken over all phases and individual experiments do not do that. Conversely, Schaefer *et al* (2004) showed experimentally that the dose to points within the PTV did not deteriorate more than 5% from the corresponding data for static irradiation even with a single-fraction (single

phase) delivery. They thus expected their variation to be even less averaged over multiple fractions.

12.3. Multiple fraction delivery

It has now been conclusively established that, if a modulated delivery is made over a course of fractions, the central limit theorem will lead to the delivered dose being the same as the convolution of the static dose distribution with the motion kernel. This is because, after a fairly small number of fractions, the motion can be described by a Gaussian function whose width decreases the more fractions occur (Bortfeld *et al* 2002a, 2002b, 2004, Chui *et al* 2003a, 2003b). This effect was also demonstrated experimentally with oscillating phantoms (Jiang *et al* 2002, 2003c, Duan *et al* 2002). This result is entirely independent of the method of IMRT delivery for reasons that are clear from the study by Webb (2005a).

Naqvi and D'Souza (2005) have developed a method to predict the effect of intrafraction motion on dose distributions in phantoms. This is a Monte Carlo method that ray-traces photons through the collimated segments for an IMRT delivery taking into account all the physics of the delivery. Moreover the isocentre of the delivery is also randomly sampled from a probability distribution. In this way the dose distribution is built up corresponding to an infinite number of treatment fractions. To verify this method, an experimental oscillating phantom was constructed which could be made to 'breath' according to a sinusoidal motion of amplitude 2 cm and period 4 s. Film was sandwiched into appropriate phantoms for ten separate occasions of IMRT delivery. These films were then digitized and converted to dose and the digital matrices, appropriately registered, were then summed to give the experimental measurement of the effect of motion sampled over ten fractions. It was shown that the theoretical predictions and the experimental curves agreed very well and from this it was not only concluded that the theoretical technique was successful but also that the interplay effects between MLC delivery and breathing motion averaged out over a complete course of radiotherapy. No conclusions could be drawn about the effect of a very limited number of fractions. Also the experimental study was limited to rigid body motion and non-Lujan-like breathing curves.

12.4. Modifying intensity modulated beams to account for motion

Deng *et al* (2001, 2002) have modelled the effect of incorporating motion into the leaf patterns for IMRT. Gierga and Jiang (2002) and Gierga *et al* (2003) evaluated the effect of organ motion by generating the leaf patterns that corresponded to a breathing lung tumour and, using Monte Carlo calculations, worked out the dose distribution corresponding to 20 different phases of leaf motion with respect to organ motion. When the average was taken, the result closely resembled the treatment plan on the PTV. Gierga *et al* (2004) did the same for liver.

12.4.1. Voxel tracking and optimization. The most advanced way being considered to track organ motion is as follows. 4D CT is performed to obtain 3D CT datasets at several (say 10) phases of the breathing cycle. Voxels are then identified in each phase and are 'tracked' by some connectivity algorithm. Examples proposed so far are optical flow solutions (Horn and Schunk 1981, El Naqa *et al* 2004, Zhang *et al* 2004a, Guerrero *et al* 2004), viscous flow solutions (Mageras *et al* 2004), finite element analysis (Brock *et al* 2004) and thinplate splines (Bookstein 1989, Schaly *et al* (2005); Rietzel *et al* 2004, Hartkens *et al* 2002, Malsch *et al* 2004, Coselmon *et al* 2004) or B splines (Blackall *et al* 2004). Then one of several things can be attempted. (i) Plans are optimized on each phase and added together with correct voxel tracking (Jiang 2004) but then the overall plan may not be optimal, (ii) plans can be created

on one phase and applied for analysis to another (Coolens *et al* 2004), (iii) a plan could be optimized overall but which may not be optimal on some particular phase (not yet attempted).

Keall *et al* (2005) made 3D CT scans at eight phases of the breathing cycle for a lung tumour patient to create a 4D CT dataset. Then morphing software was used to solve Navier Stokes' equations to transform contours made on the maximum-inhale scan to the other seven phases. The developed transform then allowed the beam's-eye-view of the PTV on the maximum-inhale phase to also morph to a different shape on the other seven phases. Then just one plan (i.e. one set of angles and weights) was made on the maximum-inhale phase and using the morphing transformation these same angles and weights were applied to the other seven phases to create in all eight dose distributions. Each plan was uniformly weighted because the breathing phases were chosen to be uniformly occupied throughout the period of breathing. This can be viewed as eight 3D plans or one 4D plan. Other work (Keall *et al* 2004a) computed these plans using Monte Carlo techniques. Then the inverse of the transform was used to add up all eight dose distributions and display them on the geometry of the maximum-inhale CT dataset.

12.4.2. DMLC tracking. Keall *et al* (2001a, 2003) have discussed synchronizing the breathing motion to the leaf motion in the dMLC technique and Keall *et al* (2001b) showed that, when the tumour 'breathed' as a rigid body and the same motion was applied to the leaves, the outcome was equivalent to irradiating the stationary tumour with the unmodified dMLC technique. Suh *et al* (2003, 2004) also irradiated an oscillating phantom using beams extracted from a patient plan with the leaves co-temporally tracking and showed that the resulting dose distribution was similar to that irradiating the static phantom. The proposal was to use 'compelled breathing' to try to maintain as regular a pattern as possible.

Keall *et al* (2004c) have studied whether a signal generated by an EPID measurement of an internal tumour marker could be used to feedback organ motion to an MLC delivering IMRT by the dMLC technique to take care of intrafraction motion. They implanted three gold cylinders, 3 mm in length and 1 mm in diameter into a lung phantom which was placed on a motion stage and set to oscillate sinusoidally with a period of 3 s and an amplitude of 4 cm. These extreme parameters were chosen to test the method in limiting conditions when the maximum velocity of the marker reached 4 cm s^{-1}. The EPID, normally acquiring an image in about 1s, was set instead to acquire in 0.1 s. However, in doing so the interval between acquisitions was still 1 s. Hence the EPID technology used by Keall *et al* (2004c) prohibited the clinical implementation of the method. A second prohibition arises because currently there is no known method to feedback motion knowledge to the (Varian) dMLC controller. Although the decreased acquisition time and the motion both degrade the image of the markers and lead to a reduction in signal-to-noise ratio from 18 to 6 compared with conventional 1 s imaging of static markers, they were able to create a marker extraction routine. In principle image extraction and feedback should allow the correction of the dMLC technique for intrafraction motion within a few years from now. The alternative method of using in-treatment-room dual-x-ray fluoroscopy has the advantages of better signal-to-noise ratio, faster continuous imaging and 3D measurement as well as permitting gating (something an EPID method cannot of course do). Conversely EPIDs are present on most accelerators (unlike in-room fluoroscopy), do not give extra patient dose and show 2D motion orthogonal to the beam which is the main source of dosimetric error, motion along the beam direction contributing little to dosimetric error.

The optimum dMLC leaf velocity patterns in the absence of motion were worked out in 1994 by three groups. Papiez (2003, 2004) has shown that there is an infinity of suboptimal solutions and worked out the corresponding solutions for targets in motion. The target executes

a rigid motion and, starting with the statement that the same equations must hold in the target frame of reference, the velocities of motion in this target frame were derived. The key conclusion, and this is vital, is that now the leaf which goes at maximum speed is *not* entirely defined by the gradient of the modulation. One or other leaf is always going at the maximum allowed velocity in this target frame that at the same time does not violate the maximum physical velocity in the lab frame. Transforms were made to obtain the velocity and position equations back in the lab frame but for a moving target. Then the motion patterns were created in which the leaves breath with the target. This construction is optimal in that the minimum treatment time will arise.

Papiez and Rangaraj (2005) extended the analysis for elastic body motion and provided the optimal solution in terms of minimal treatment time (see also Rangaraj and Papiez (2005) and Papiez *et al* (2005)). Alternatively Webb (2005a) transformed the unbreathing leaf trajectory plots and created a perfectly practical solution which is one of the suboptimal ones. Papiez' solutions did not address the issue of phase mismatch between organ motion and leaf motion whereas Webb (2005a) concentrated on this aspect considerably. The studies of both Webb (2005a) and Papiez (2003, 2004) and Papiez and Rangaraj (2005) are solutions of the 1D leaf velocity problem whereby leaf-pairs can be considered separately. The complication of change of density of tissue and change of density of interactions is so far ignored in these complex mathematical studies but was addressed by Webb (2006a). The solutions also only work for regular rhythmical motion although Papiez *et al* (2005) have considered adapting to variable motion. None of these studies have yet considered transmission, scatter, leaf end issues. D'Souza *et al* (2005) made experimental measurements using a motion of the couch instead of the MLC whereby the couch motion mirrored that of the patient. Webb (2005b) showed that inventing pseudo-profiles which when sampled by motion would give the correctly required profiles does not work because of ill-conditioning and the need for negative intensities.

Nill *et al* (2005) showed that kVCT systems either in-line with the MV beam or at right angles to it can be used to track intrafraction organ motion at right angles to the detector.

12.5. Predicting the future

Any breathing-control method that uses either (i) gating, (ii) breathhold or (iii) full tracking must be able to make adjustments to the treatment based on measurement at some time t_1 (or series of times up to t_1) that can give a measure of the target position at some future time $t_2 > t_1$ with the collimation adjusted for t_2 not t_1. Hence some kind of computer prediction of the future is required. Vedam *et al* (2004) have made measurements of diaphragmatic breathing for a 'signal history length (SHL)' of between 1 s and 7 s, in intervals of 1 s and predicted the future target position for a future time Δ between 0 s and 1.8 s (in intervals of 0.2 s). They developed two types of prediction algorithm, one based on fitting a sinusoid to the SHL data and the other based on an adaptive filter. They then computed the expected position of the target at some time interval Δ in the future and compared this with the actual position to generate an error in position. For data of different lengths they then computed the standard deviation of this error and plotted it as a function of the SHL and of Δ. This was done for data (i) with the patient free breathing, (ii) with audio coaching and (iii) with visual coaching. It was determined that for all cases (i) the computer predictions were better than making no predictions, (ii) the adaptive filter worked best. It was also determined that (iii) the standard deviation error could be kept to 2 mm provided a SHL of 5 s was used and prediction was no further than $\Delta = 0.4$ s into the future. Otherwise the error increased with increasing Δ and with decreasing SHL. Jin and Yin (2005) have shown the measured time delay for a Varian

linac-based gating system was 0.17 s. Kakar *et al* (2005) have used adaptive neuro fuzzy inference (ANFIS) to predict future motion from observed motion. Webb (2006b) deduced the dosimetric effect of latency.

13. Summary and conclusions

The present research position with respect to accounting for tissue motion is vibrant, active and expanding. There is a mixture of quite disparate approaches. There are a few commercial products but limited clinical implementation.

Acknowledgments

I should like to thank Phil Evans, Eleni Nioutsikou and Dualta McQuaid for reading a draft manuscript and making helpful suggestions.

References

Alheit H, Dornfeld S, Winkler C, Blank H and Geyer P 2000 Stereotactic guided irradiation in prostatic cancer using the ExacTrac-System (BrainLab) *Radiother. Oncol.* **56** (Suppl. 1) S107

Allen A M, Siracuse K M, Hayman J A and Balter J M 2004 Evaluation of the influence of breathing on the movement and modeling of lung tumors *Int. J. Radiat. Oncol. Biol. Phys.* **58** 1251–7

Artignan X, Smitsmans M H P, de Bois J, Lebesque J V, van Herk M and Bartelink H 2002 On-line ultrasound-image guidance for radiotherapy of prostate cancer: the impact of image acquisition on prostate displacement *Radiother. Oncol.* **64** (Suppl. 1) S279

Artignan X, Smitsmans M H P, Lebesque J V, Jaffray D A, van Herk M and Bartelink H 2004 Online ultrasound image guidance for radiotherapy of prostate cancer: impact of image acquisition on prostate displacement *Int. J. Radiat. Oncol. Biol. Phys.* **59** 595–601

Aubrey J-F, Beaulieu L, Girouard L-M, Aubin S, Tremblay D, Laverdiere J and Vigneault E 2004 Measurements of intrafraction motion and interfraction and intrafraction rotation of prostate by three-dimensional analysis of daily portal imaging with radiopaque markers *Int. J. Radiat. Oncol. Biol. Phys.* **60** 30–9

Aznar M C, Sixel K E and Ung Y C 2000 Feasibility of deep inspiration breath hold combined with intensity modulated radiation treatment delivery for left sided breast cancer *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 297

Balter J M, Litzenberg D W, Brock K K, Sanda M, Sullivan M, Sandler H M and Dawson L A 2000 Ventilatory movement of the prostate during radiotherapy. *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 167

Balter J, Wright N, Dimmer S, Friemel B, Newell J, Cheng Y and Mate T 2003 Demonstration of accurate localisation and continuous tracking of implantable wires *Int. J. Radiat. Oncol. Biol. Phys.* **57** S264

Balter J M, Wright J N, Newell L J, Friemel B, Dimmer S, Cheng Y, Wong J, Vertatschitsch E and Mate T P 2005 Accuracy of a wireless localization system for radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **61** 933–7

Barnes E A, Murray B R, Robinson D M, Underwood L J, Hanson J and Roa W H Y 2001 Dosimetric evaluation of lung tumour immobilization using breath hold at deep inspiration *Int. J. Radiat. Oncol. Biol. Phys.* **50** 1091–8

Berbeco R I, Mostafavi H, Sharp G C and Jiang S B 2005a Towards fluoroscopic respiratory gating for lung tumours without radiopaque markers *Phys. Med. Biol.* **50** 4481–90

Berbeco R I, Neicu T, Rietzel E, Chen G T Y and Jiang S B 2005b A technique for respiratory-gated radiotherapy treatment verification with an EPID in *cine* mode *Phys. Med. Biol.* **50** 3669–79

Berbeco R I, Nishioka S, Shirato H, Chen G T Y and Jiang S B 2005c Residual motion of lung tumours in gated radiotherapy with external respiratory surrogates *Phys. Med. Biol.* **50** 3655–67

Beyer D, Quiet C, Rogers K and Gurgoze E 2000 Prostate motion during a course of IMRT: the value of daily ultrasound to guide portal localization and correct for random and systematic errors *Radiother. Oncol.* **56** (Suppl. 1) S105

Bignardi M, Galelli M, Spiazzi L, Bonetti M and Magrini S M 2000 Conformal radiotherapy for prostate carcinoma: differences in dose distribution between the original plan and the same plan recalculated (in the same patient) after 3 and 6 weeks of treatment *Radiother. Oncol.* **56** (Suppl. 1) S108

Blackall J, Ahmad S, Miquel M E, Landau D and Hawkes D 2004 Techniques for constructing breathing motion models for 4D radiotherapy planning in lung cancer *Radiother. Oncol.* **73** (Suppl. 1) S361–2

Bookstein F 1989 Principal Warps: Thin plate splines and the decomposition of deformations *IEE Trans. Pattern. Anal. Mach. Intell.* **11** 567–85

Bortfeld T, Jiang S B and Rietzel E 2004 Effects of motion on the total dose distribution *Semin. Radiat. Oncol.* **14** 41–51

Bortfeld T, Jokivarsi K, Goitein M and Jiang S 2002a Effects of intra-fraction motion on IMRT delivery with MLC, compensators and scanning *Med. Phys.* **29** 1347

Bortfeld T, Jokivarsi K, Goitein M, Kung J and Jiang S B 2002b Effects of intra-fraction motion on IMRT dose delivery: statistical analysis and simulation *Phys. Med. Biol.* **47** 2203–20

Bortfeld T, van Herk M and Jiang S B 2002c When should systematic patient positioning errors in radiotherapy be corrected? *Phys. Med. Biol.* **47** N297–N302

Bouchet L G, Marks S L, Bova F J, Goodchild G, Buatti J M and Friedmena W A 2000 Three-dimensional ultrasound optic guidance for high precision radiation therapy *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 195

Brock K K, Sharpe M B and Jaffray D A 2004 Biomechanical modelling of anatomical deformation for image-guided registration of soft-tissue surrogates *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 467–71

Butler L E, Forster K M, Stevens C W, Bloch C, Liu H H, Tucker S L, Komaki R, Liao Z and Starkschall G 2004 Dosimetric benefits of respiratory gating: a preliminary study *J. Clin. Appl. Med. Phys.* **5** 1–9

Chandra A, Dong L, Huang E, Kuban D A, O'Neill L J, Rosen I I and Pollack A 2001 Evaluation of ultrasound-based daily prostate localization during IMRT for prostate cancer *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 167–8

Chandra A, Dong L, Huang E, Kuban D A, O'Neill L, Rosen I and Pollack A 2003 Experience of ultrasound-based daily prostate localization *Int. J. Radiat. Oncol. Biol. Phys.* **56** 436–47

Christian J A, McNair H A, Symonds-Tayler J R N, Knowles C, Bedford J L and Brada M 2003 Reduction in lung tumour motion using active breathing control *Radiother. Oncol.* **68** (Suppl. 1) S115

Chui C, LoSasso T and Palm A 2003a Computational and empirical verification of intensity modulated radiation therapy delivered with a multileaf collimator *Proc. World Congress in Medical Physics (Sydney, Australia)* CDROM and website only

Chui C-S, Yorke E and Hong 2003b The effects of intra-fraction organ motion on the delivery of intensity-modulated field with a multileaf collimator *Med. Phys.* **30** 1736–46

Coolens C, Evans P M, Seco J, Webb S, Blackall J, Rietzel E and Chen G T Y 2004 Susceptibility of IMRT dose distributions to deformable organ motion and the impact of beam smoothing *Radiother. Oncol.* **73** (Suppl. 1) S176–7

Coselmon M M, Balter J M, McShan D L and Kessler M L 2004 Mutual information based CT registration of the lung at exhale and inhale breathing states using thin-plate splines *Med. Phys.* **31** 2942–8

Court L E, Dong L, Lee A K, Cheung R, Bonnen M D, O'Daniel J, Wang H, Mohan R and Kuban D 2005 An automatic CT-guided adaptive radiation therapy technique by online modification of multileaf collimator leaf positions for prostate cancer *Int. J. Radiat. Oncol. Biol. Phys.* **62** 154–63

Dawson L A, Brock K, Litzenberg D, Kazanjian S, McGinn C G, Lawrence T S, Ten Haken R K and Balter J 2000 The reproducibility of organ position using active breathing control (ABC) during liver radiotherapy *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **4** (Suppl.) 1675

D'Souza W D, Naqvi S A and Yu C X 2005 Real-time intra-fraction-motion tracking using the treatment couch: a feasibility study *Phys. Med. Biol.* **50** 4021–33

Della Biancia C, Yorke E, Mageras G, Giraud P, Rosenzweig K, Amols H and Ling C 2003 Comparison of two breathing levels for gated intensity modulated radiation therapy (IMRT) of lung cancer *Med. Phys.* **30** 2340–1

Deng J, Guerrero T, Ding M S, Jolly J, Pawlicki T and Ma C M 2001 Incorporate organ motion into MLC leaf sequencing for intensity modulated radiation therapy *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 92–3

Deng J, Lee M, Ding M and Ma C 2002 Effect of breathing motion on IMRT treatment of breast cancer: a Monte Carlo study *Med. Phys.* **29** 1263

Dietrich L, Tücking T, Nill S and Oelfke U 2005 Compensation for respiratory motion by gated radiotherapy: an experimental study *Phys. Med. Biol.* **50** 2405–14

Díez S, Garcia J and Sendra F 2004 Analysis and evaluation of periodic physiological organ motion in radiotherapy treatments *Radiother. Oncol.* **73** 325–9

Dong L, Court L, Wang H, Daniel J O and Mohan R 2004 Image-guided radiotherapy with in-room CT-on-rails *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 18–9

Donovan E M, McNair H A, Eagle S, Shoulders B, Clements N, Evans P M, Symonds-Tayler J R N and Yarnold J R 2003 Minimizing cardiac irradiation in breast radiotherapy with an automatic breathing control device: initial findings *Clin. Oncol.* **15** (Suppl. 2) S14

Donovan E M, McNair H, Evans P M, Symonds-Tayler R and Yarnold J R 2002 Initial experience with an automatic breathing control device in breast radiotherapy *Radiother. Oncol.* **64** (Suppl. 1) S45

Duan J, Shen S, Fiveash J, Brezovich I, Popple R and Pareek P 2002 Impact of dose fractionation on dosimetric errors induced by respiratory motions during IMRT delivery: a 3-D volumetric dose measurement approach *Med. Phys.* **29** 1346

El Naqa I, Low D A, Nystrom M, Parikh P, Lu W, Deasy J O, Amini A, Hubenschmidt J and Wahab S 2004 An optical flow approach for automated breathing motion tracking in 4D computed tomography *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 74–7

Engelsman M, Sharp G C, Bortfeld T, Onimaru R and Shirato H 2005 How much margin reduction is possible through gating or breath hold? *Phys. Med. Biol.* **50** 477–90

Falco T, Evans M D C, Shenouda G and Podgorsak E B 2001 Ultrasound imaging for external beam prostate treatment setup and dosimetric verification *Med. Phys.* **28** 1988

Fraass B A, McShan D L, Vineberg K A, Balter J, Ten Haken R K and Eisbruch 2002 Generation of robust IMRT plans for head/neck cancer: replacing the PTV with direct accommodation of setup uncertainty and buildup region dosimetry *Radiother. Oncol.* **64** (Suppl. 1) S96

Frazier R C, Vicini F A, Sharpe M B, Fayad J, Yan D, Martinez A A and Wong J W 2000 The impact of respiration on whole breast radiotherapy: a dosimetric analysis using active breathing control *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 200

Frazier R C, Vicini F A, Sharpe M B, Yan D, Fayad J, Baglan K L, Kestin L L, Remouchamps V M, Martinez A A and Wong J W 2004 Impact of breathing motion on whole breast radiotherapy: a dosimetric analysis using active breathing control *Int. J. Radiat. Oncol. Biol. Phys.* **58** 1041–7

George R, Keall P J, Kini V R, Vedam S S, Siebers J V, Wu Q, Lauterbach M H, Arthus D W and Mohan R 2003 Quantifying the effect of intrafraction motion during breast IMRT planning and dose delivery *Med. Phys.* **30** 552–62

George R, Vedam S S, Chung T D, Ramakrishnan V and Keall P J 2005 The application of the sinusoidal model to lung cancer patient respiratory motion *Med. Phys.* **32** 2850–61

Gierga D P, Brewer J, Sharp G C, Betke M, Willett C G and Chen G T Y 2005 The correlation between internal and external markers for abdominal tumors: implications for respiratory gating. *Int. J. Radiat. Oncol. Biol. Phys.* **61** 1551–8

Gierga D, Chen G, Kung J, Betke M, Lombardi J and Willett C 2003 Quantitative fluoroscopy of respiration-induced abdominal tumor motion on IMRT dose distributions *Med. Phys.* **30** 1340

Gierga D P, Chen G T Y, Kung J H, Betke M, Lombardi J and Willett C G 2004 Quantification of respiration-induced abdominal tumor motion and its impact on on IMRT dose distributions *Int. J. Radiat. Oncol. Biol. Phys.* **58** 1584–95

Gierga D and Jiang S 2002 A Monte Carlo study on the interplay effect between MLC leaf motion and respiration-induced tumor motion in lung IMRT delivery *Med. Phys.* **29** 1266

Giraud P, Helfre S, Servois V, Dubray B, Beigelman-Grenier C P, Zalcman-Liwartoski G A, Straus-Zelter C M, Neuenschwander S, Rosenwald J C and Cosset J M 2000 Evaluation of intrathoracic organs mobility using CT gated by a spirometer *Radiother. Oncol.* **56** (Suppl. 1) S39

Guerrero T, Zhang G, Huang T-C and Lin K-P 2004 Intrathoracic tumour motion estimation from CT imaging using the 3D optical flow method *Phys. Med. Biol.* **49** 4147–61

Hagekyriakou J, Song G L and Sephton R G 2000 The accuracy of an ultrasound guidance system for positioning the prostate at radiotherapy *Radiother. Oncol.* **56** (Suppl. 1) S38

Hartkens T, Rueckert D, Schnabel J A, Hawkes D J and Hill D L G 2002 *VTK CISG Registration Toolkit: An Open Source Software for Affine and Non-rigid Registration of Single and Multiple 3D Images BVM 2002* (Leipzig: Springer)

Héon J, Falco T, Shenouda G, Duclos M, Faria S and Souhami L 2002 Ultrasound imaging for external beam prostate treatment setup *Radiother. Oncol.* **64** (Suppl. 1) S45

Herman M G, Rosenzweig D P and Hendee W R 2003 Every patient receiving 3D or IMRT must have image-based target localization prior to turning on the beam *Med. Phys.* **30** 287–9

Holmberg O, Kasenter A, Verdugo V, Buckney S, Gribben A, Hollywood D and McClean B 2000 Temporal uncertainties of target volumes in step-and-shoot IMRT: a numerical simulation *Radiother. Oncol.* **56** (Suppl. 1) S108

Hoogeman M S, van Herk M, de Bois J, Boersma L J, Koper P C M and Lebesque J V 2003 Strategies to reduce the systematic error due to tumor motion in radiotherapy of prostate cancer *Physica Medica* **19** 54–5

Horn B K P and Schunk B G 1981 Determining optical flow *Artif. Intell.* **17** 185–204

Huang E, Dong L, Chandra A, Kuban D A, Rosen I I, Evans A and Pollack A 2002 Intrafraction prostate motion during IMRT for prostate cancer *Int. J. Radiat. Oncol. Biol. Phys.* **53** 261–8

Hugo G D, Agazaryan N and Solberg T D 2002 An evaluation of gating window size, delivery method, and composite field dosimetry of respiratory-gated IMRT *Med. Phys.* **29** 2517–25

Hugo G, Solberg T, Demarco J, Paul T, Agazaryan N, Arellano A and Smathers J 2001 Preliminary dosimetric investigations into gated IMRT *Med. Phys.* **28** 1294

Jiang S 2004 Tracking tumor with dynamic MLC: Be SMART *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* p 47

Jiang S B and Doppke K 2001 Dosimetric effect of respiratory motion on the treatment of breast cancer with tangential fields *Med. Phys.* **28** 1228

Jiang S B, Pope C, Al Jarrah K M, Kung J H, Bortfeld T and Chen G T Y 2003 An experimental investigation on intra-fractional organ motion effects in lung IMRT treatments *Phys. Med. Biol.* **48** 1773–84

Jiang S, Rivinius C, Al Jarrah K, Kung J, Bortfeld T and Chen G 2002 An experimental investigation on interplay effect between DMLC leaf motion and respiration-induced tumor motion in lung IMRT treatment *Med. Phys.* **29** 1347

Jin J-Y and Yin F-F 2005 Time delay measurement for linac based treatment delivery in synchronised respiratory gating radiotherapy *Med. Phys.* **32** 1293–6

Kakar M, Nyström H, Aarup L R, Nøttrup T J and Olsen D R 2005 Respiratory motion prediction by using the adaptive neuro fuzzy inference system (ANFIS) *Phys. Med. Biol.* **50** 4721–8

Keall P 2004 Four-dimensional computed tomography imaging and treatment planning *Semin. Radiat. Oncol.* **14** 81–90

Keall P J, Joshi S, Vedam S S, Siebers J V, Kini V R and Mohan R 2005 Four-dimensional radiotherapy planning for DMLC-based respiratory motion tracking *Med. Phys.* **32** 942–51

Keall P, Kini V, Vedam S and Mohan R 2001a 4D IMRT: dosimetric and practical considerations *Med. Phys.* **28** 1252

Keall P, Kini V, Vedam S and Mohan R 2001b Motion adaptive x-ray therapy: a feasibility study *Phys. Med. Biol.* **46** 1–10

Keall P J, Siebers J V, Joshi S and Mohan R 2004a Monte-Carlo as a four-dimensional radiotherapy treatment-planning tool to account for respiratory motion *Phys. Med. Biol.* **49** 3639–48

Keall P J, Starkshall G, Shukla H, Forster K M, Ortiz V, Stevens C W, Vedam S S, George R, Guerrero T and Mohan R 2004b Acquiring 4D thoracic CT scans using a multislice helical method *Phys. Med. Biol.* **49** 2053–67

Keall P, Todor A D, Vedam S S, Bartee C L, Siebers J V and Kini V R 2004c On the use of EPID-based implanted marker tracking for 4D radiotherapy *Med. Phys.* **31** 3492–99

Keall P, Vedam S, George R, Kinl V and Mohan R 2002 4D IMRT: a phantom study *Radiother. Oncol.* **64** (Suppl. 1) S261

Keall P, Wu Q, Wu Y and Kim J O 2003 Dynamic MLC IMRT *IMRT—the state of the art: AAPM Medical Physics Monograph Number 29* ed J R Palta and T R Mackie (Madison, WI: Medical Physics Publishing) pp 319–71

Kim S, Akpati H C, Kielbasa J E, Li J G, Liu C, Amdur R J and Palta J R 2004 Evaluation of intrafraction patient movement for CNS and head and neck IMRT *Med. Phys.* **31** 500–6

Kim D J W, Murray B R, Halperin R and Roa W H Y 2001 Held-breath self-gating technique for radiotherapy of non-small-cell lung cancer: A feasibility study *Int. J. Radiat. Oncol. Biol. Phys.* **49** 43–9

Kini V R, Keall P J, Vedam S S, Arthur D W, Kavanagh B D, Cardinale R M and Mohan R 2000 Preliminary results from a study of a respiratory motion tracking system: underestimation of target volume with conventional CT simulation *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 164

Kini V R, Vedam S S, Keall P J and Mohan A R 2001 A dynamic non-invasive technique for predicting organ motion in respiratory-gated radiotherapy of the chest *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 25

Kitamura K, Shirato H, Seppenwoolde Y, Onimaru R, Oda M, Fujita K, Shimizu S, Shinohara N, Harabayashi T and Miyasaka K 2002 Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions *Int. J. Radiol. Oncol. Biol. Phys.* **53** 1117–23

Kubo H D and Wang L 2000 Compatibility of Varian 2100C gated operations with enhanced dynamic wedge and IMRT dose delivery *Med. Phys.* **27** 1732–8

Kung J H, Zygmanski P, Kooy H and Chen G 2000 Dose error in IMRT treatment of lung cancer without respiratory gating *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 344

Kuriyama K, Onishi H, Sano N, Komiyama T, Aikawa Y, Tateda Y, Araki T and Uematsu M 2003 A new irradiation unit constructed of self-moving gantry-CT and linac *Int. J. Radiat. Oncol. Biol. Phys.* **55** 428–35

Langen K M and Jones D T L 2001 Organ motion and its management. *Int. J. Radiat. Oncol. Biol. Phys.* **50** 265–78

Langen K M *et al* 2003 Evaluation of ultrasound-based localization for image-guided radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **57** 635–44

Large C, Brumley K and Ramsey C 2001 The dosimetric consequences of intra-fraction prostate motion in intensity modulation *Med. Phys.* **28** 1253

Lattanzi J, McNeeley S, Donnelly S, Palacio E, Hanlon A, Schultheiss T E and Hanks G E 2000 Ultrasound based stereotactic guidance in prostate cancer-quantification of organ motion and set-up errors in external beam radiotherapy *Comput. Aided Surg.* **5** 289–95

Li J and Xing L 2000b Inverse planning incorporating organ motion *Proc. World Congress of Medical Physics and the AAPM Annual Congress, August 2000* paper FR-EaBR-10

Little D J, Dong L, Levy L B, Chandra A and Kuban D A 2003 Use of portal images and BAT ultrasonography to measure setup error and organ motion for prostate IMRT: implications for treatment margins *Int. J. Radiat. Oncol. Biol. Phys.* **56** 1218–24

Loof M, Engstrom P, Uttman K and Nystrom H 2001 Optimisation of IMRT: can geometrical uncertainties be incorporated into the optimisation process? *Radiother. Oncol.* **61** (Suppl. 1) S66

Lujan A E, Balter J M and Ten Haken R K 2003 A method for incorporating organ motion due to breathing into 3D dose calculations in the liver: sensitivity to variations in motion *Med. Phys.* **30** 2643–9

Lyatskaya Y, Chin L, Harris J and Lu H 2002 Accurate patient position control for breast cancer treatment using respiratory manoeuvres *Med. Phys.* **29** 1239

Macpherson M, Crljenko T, Vo D, El-Hakim S and Gerig L 2002 A machine-vision based radiotherapy gating device *Med. Phys.* **29** 1213

Mageras G 2004 When is a deep inspiration breath-hold technique during external beam radiotherapy beneficial? *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* p 52

Mageras G S 2001 Respiratory gating in conformal radiotherapy *Radiother. Oncol* **61** (Suppl. 1) S35

Mageras G *et al* 2004 Evaluation of an automated deformable matching method for quantifying lung tumor motion in respiration correlated CT images *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 364–7

Mageras G S and Yorke E 2004 Deep inspiration breath hold and respiratory gating strategies for reducing organ motion in radiation treatment *Semin. Radiat. Oncol.* **14** 65–75

Mah D, Hanley J, Rosenzweig K E, Yorke E, Braban L, Ling C C, Leibel S A and Mageras G 2000 Technical aspects of the deep inspiration breath-hold technique in the treatment of thoracic cancer *Int. J. Radiat. Oncol. Biol. Phys.* **48** 1175–85

Malsch U, Frühling C and Bendl R 2004 Methods for elastic adaptation of segmented volumes of interest for adaptive radiotherapy planning *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 69–73

Martinez A A, Yan D, Lockman D, Brabbins D, Kota K, Sharpe M, Jaffray D A, Vicini F and Wong J 2001 Improvement in dose escalation using the process of adaptive radiotherapy combined with three-dimensional conformal or intensity-modulated beams for prostate cancer *Int. J. Radiat. Oncol. Biol. Phys.* **50** 1226–34

McNair H, Christian J, Knowles C, Symonds-Tayler J and Brada M 2003 Can the active breathing co-ordinator be used for patients receiving radical lung radiotherapy? *Radiother. Oncol.* **68** (Suppl. 1) S47

McNeeley S, Buyyounouski M, Price R, Horwitz E and Ma C 2003 The use of ultrasound in target localization *Radiother. Oncol.* **68** (Suppl. 1) S16

McShan D, Lynn K, Vineberg K and Fraass B 2002 Radiotherapy plan optimisation accounting for set-up and motion uncertainty using a multiple instance geometry approximation *Med. Phys.* **29** 1257

McShan D, Ten Haken R, Kessler M, Balter J, Lam K and Fraass B 2001 Radiotherapy plan optimisation accounting for set-up and motion uncertainty using a multiple instance geometry approximation *Radiother. Oncol.* **61** (Suppl. 1) S13

Mechalakos J G, Mageras G S, Zelefsky M J, Lyass O, van Herk M, Kooy H M, Leibel S A and Ling C C 2002 Time trends in organ position and volume in patients receiving prostate three-dimensional conformal radiotherapy *Radiother. Oncol.* **62** 261–5

Moore C J and Graham P A 2000 3D dynamic surface sensing and CT-body matching: a tool for patient set-up and monitoring in radiotherapy *Comput. Aided Surg.* **5** 234–45

Morr J, DiPetrillo T, Tsai J and Wazer D 2000 Clinical use of daily transabdominal ultrasound localization with intensity modulated radiation therapy (IMRT) for prostate cancer *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) p 308

Morr J, DiPetrillo T, Tsai J-S, Engler M and Wazer D E 2002 Initial experience with ultrasound localization for positioning prostate cancer patients for external beam radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **53** 1124–9

Muench R K, Seiler P G and Verwey J 2001 Application of magnetic tracking for the continuous precise measurement of tumour positions in conformal radiotherapy *Physica Medica* **17** 164

Murphy M J, Chang S D, Gibbs I C, Le Q-T, Hai J, Kim D, Martin D P and Adler J R 2003 Patterns of patient movement during frameless image-guided radiosurgery *Int. J. Radiat. Oncol. Biol. Phys.* **55** 1400–8

Naqvi S A and D'Souza W D 2005 A stochastic convolution/superposition method with isocentre sampling to evaluate intrafraction motion effects in IMRT *Med. Phys.* **32** 1156–63

Nederveen A J, van der Heide U A, Dehnad H, Jeroen R, van Moorselaar A, Hofman P and Lagendijk J J W 2002 Measurements and clinical consequences of prostate motion during a radiotherapy fraction *Int. J. Radiat. Oncol. Biol. Phys.* **53** 206–14

Nelson C, Starkschall G, Balter P, Fitzpatrick M J, Antolak J A, Tolani N and Prado K 2005 Respiration-correlated treatment delivery using feedback-guided breath hold: a technical study *Med. Phys.* **32** 175–81

Nill S, Unkelbach J, Dietrich L and Oelfke U 2005 Online correction for respiratory motion: evaluation of two different imaging geometries *Phys. Med. Biol.* **50** 4087–96

Nioutsikou E, Webb S, Panakis N, Bortfeld T R and Oelfke U 2005 Reconsidering the definition of a dose volume histogram *Phys. Med. Biol.* **50** L17–L19

Nøttrup T, Korreman S, Aarup L, Olsen M, Pedersen A, Specht L and Nyström H 2005 Changes in respiratory pattern during curative radiotherapy for lung cancer *Radiother. Oncol.* **76** (Suppl. 2) S74–75

Padhani A R, Khoo V S and Suckling J 1999 Evaluating the effect of rectal distension and rectal movement on the prostate gland position using cine MRI *Int. J. Radiat. Oncol. Biol. Phys.* **44** 525–33

Palta J R and Mackie T R (eds) 2003 *Intensity Modulated Radiation Therapy—the State of the Art* (Madison, WI: Medical Physics Publishing)

Papiez L 2003 The leaf sweep algorithm for an immobile and moving target as an optimal control problem in radiotherapy delivery *Math. Comp. Modell.* **37** 735–45

Papiez L 2004 DMLC leaf-pair optimal control of IMRT delivery for a moving rigid target *Med. Phys.* **31** 2742–54

Papiez L and Rangaraj D 2005 DMLC leaf-pair optimal control for mobile, deforming target *Med. Phys.* **32** 275–85

Papiez L, Rangaraj D and Keall P 2005 Real-time DMLC IMRT delivery for mobile and deforming targets *Med. Phys.* **32** 3037–48

Paskalev K, Ma C, Jacob R and Price R 2003 Daily target localization based on 3D image correlation *Med. Phys.* **30** 1337

Paskalev K, Ma C-M, Jacob R, Price R, McNeeley S, Wang L, Movsas B and Pollack A 2004 Daily target localization for prostate patients based on 3D image correlation *Phys. Med. Biol.* **49** 931–9

Pavel L, Rowbottom C G, Hector C, Partridge M and Bortfeld T 2001 Estimation of the effects of movements on dose distribution for prostate patients *Radiother. Oncol.* **61** (Suppl. 1) S36

Plasswilm L, Alber M, Paulsen F, Bakal A, Birkner M, Glocker S, Christ G, Buck C, Nůsslin F and Bamberg M 2002 First clinical experience with image-guided intensity modulated radiation treatment of prostate cancer patients *Radiother. Oncol.* **64** (Suppl. 1) S271

Ramsey C R, Large C, Scaperoth D, Arwood D and McDonald W 2001 The dosimetric consequences of intra-fraction prostate motion in intensity modulation *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 214

Ramsey C R, Scaperoth D and Arwood D 2000 Clinical experience with a commercial respiratory gating system *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 164

Rangaraj D and Papiez L 2005 Synchronized delivery of DMLC intensity modulated radiation therapy for stationary targets *Med. Phys.* **32** 1802–17

Remouchamps V M, Vicini F A, Martinez A A, Sharpe M B, Kestin L L and Wong J W 2002 Reductions in heart and lung doses using deep inspiration breath hold with active breathing control and IMRT for patients treated with locoregional breast irradiation *Radiother. Oncol.* **64** (Suppl. 1) S139

Remouchamps V M, Vicini F A, Sharpe M B, Kestin L L, Martinez A A and Wong J W 2003 Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation *Int. J. Radiat. Oncol. Biol. Phys.* **55** 392–406

Rietzel E, Chen G T Y, Adams J A, Hernandez A H and Willett C G 2004 Treatment planning including respiratory motion based on 4D computed tomography data *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 27–31

Sawada A, Yoda K, Kokubo M, Nagata Y and Hiraoka M 2002 Non-invasive respiratory gated radiation treatment system based on a 3D ultrasound device and a 3D digital localizer *Med. Phys.* **29** 1310

Sawada A, Yoda K, Kokubo M, Nagata Y and Hiraoka M 2004 A technique for noninvasive respiratory gated radiation treatment system based on a real time 3D ultrasound image correlation: a phantom study *Med. Phys.* **31** 245–50

Schaefer M, Munter M W, Thilmann C, Sterzing F, Haering P, Combs S E and Debus J 2004 Influence of intra-fractional breathing movement in step-and-shoot IMRT *Phys. Med. Biol.* **49** N175–N179

Schaly B, Bauman G S, Battista J J and Van Dyke J 2005 Validation of contour-driven thin-plate splines for tracking fraction-to-fraction changes in anatomy and radiation therapy dose mapping *Phys. Med. Biol.* **50** 459–75

Schaly B, Kempe J A, Bauman G S, Battista J J and van Dyke J 2004 Tracking the dose distribution in radiation therapy by accounting for variable anatomy *Phys. Med. Biol.* **49** 791–805

Schweikard A and Adler J R 2000 Motion tracking for respiratory motion in radiosurgery *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 166

Schweikard A, Shiomi H and Adler J 2004 Respiration tracking in radiosurgery *Med. Phys.* **31** 2738–41

Seiler P G, Blattmann H, Kirsch S, Muench R K and Schilling Ch 2000 A novel tracking technique for the continuous precise measurement of tumour positions in conformal radiotherapy *Phys. Med. Biol.* **45** N103–N110

Seppenwoolde Y, Shirato H, Kitamura K, Shimizu S, van Herk M, Lebesque J V and Miyasaka K 2001 3D Tumor motion in lung due to breathing and heartbeat, measured during real-time tumor tracking radiation therapy *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 24

Seppenwoolde Y, Shirato H, Kitamura K, Shimizu S, van Herk M, Lebesque J V and Miyasaka K 2002 Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **53** 822–34

Sharp G, Jiang S B, Ruan D, Castanon and Shirato H 2003 Evaluation of prediction methods for real-time tumor tracking during treatment *Med. Phys.* **30** 1346

Shimizu S, Shirato H, Kitamura K, Ogura S, Akita-Dosaka H, Tateishi U, Watanabe Y, Fujita K, Shimizu T and Miyasaka K 2000 Fluoroscopic real-time tumor-tracking radiation treatment (RTRT) can reduce internal margin (IM) and set-up margin (SM) of planning target volume (PTV) for lung tumors *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 166

Shimizu S, Shirato H, Ogura S, Akita-Dosaka H, Kitamura K, Nishioka T, Kagei K, Nishimura M and Miyasaka K 2001 Detection of lung tumour movement in real-time tumour-tracking radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **51** 304–10

Shirato H, Oita M, Fujita K, Watanabe Y and Miyasaka K 2004b Feasibility of synchronization of real-time tumor-tracking radiotherapy and intensity-modulated radiotherapy from viewpoint of excessive dose from fluoroscopy *Int. J. Radiat. Oncol. Biol. Phys.* **60** 335–41

Shirato H *et al* 2000a Physical aspects of a real-time tumor-tracking system for gated radiotherapy *Int. J. Radiat. Oncol. Biol. Phys.* **48** 1187–95

Shirato H *et al* 2000b Four-dimensional treatment planning and fluoroscopic real-time tumor tracking radiotherapy for moving tumour *Int. J. Radiat. Oncol. Biol. Phys.* **48** 435–42

Shirato H, Seppenwoolde Y, Kitamura K, Onimura R and Shimizu S 2004a Intrafractional tumor motion: lung and liver *Semin. Radiat. Oncol.* **14** 10–8

Sixel K E, Aznar M C and Ung Y C 2001 Deep inspiration breath hold to reduce irradiated heart volume in breast cancer patients *Int. J. Radiat. Oncol. Biol. Phys.* **49** 199–204

Sohn J W, Low D A and Deasy J O 2001 Motion-induced distribution artefacts in lung cancer IMRT *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 347–8

Solberg T 2000 Development and modification of a virtual source model for Monte Carlo based IMRT verification *Proc. World Congress of Medical Physics and the AAPM Annual Congress (August 2000)* Paper WE-B309-03

Sonke J-J, Zijp L, Remeijer P and van Herk M 2005 Respiratory correlated cone beam CT *Med. Phys.* **32** 1176–86

Spitters-Post I, van der Vight L P, van Lin E N J T and Visser A G 2002 The use of fiducial (gold) markers for monitoring prostate movements during radiation therapy *Radiother. Oncol.* **64** (Suppl. 1) S44

Stromberg J S, Sharpe M B, Kim L H, Kini V J, Jaffray D A, Martinez A A and Wong J W 2000 Active breathing control (ABC) for Hodgkin's disease: reduction in normal tissue irradiation with deep inspiration and implications for treatment *Int. J. Radiat. Oncol. Biol. Phys.* **48** 797–806

Suh Y, Yi B, Ahn S, Kim J, Lee S, Shin S and Choi E 2004 Aperture maneuver with compelled breath (AMC) for moving tumors: a feasibility study using moving phantom *Med. Phys.* **31** 760–6

Suh Y, Yi B, Ahn S, Lee S, Kim J, Shin S and Choi E 2003 Adaptive field shaping to moving tumor with the compelled breath control: a feasibility study using moving phantom *Proc. World Congress in Medical Physics (Sydney, Australia)* CDROM and website only

Tomé W A, Meeks S L, McNutt T R, Buatti J M, Bova F J, Friedman W A and Mehta M 2001 Optically guided intensity modulated radiotherapy *Radiother. Oncol.* **61** 33–44

Tomé W A, Mehta M P, Meeks S L, Buatti J M, Bova F J and Friedman W A 2000 Image guided fractionated stereotactic radiotherapy *Radiother. Oncol.* **56** (Suppl. 1) S60

Trichter F and Ennis R D 2001 Patient positioning in prostate IMRT: advantages of BAT over EPID *Med. Phys.* **28** 1292

Unkelbach J and Oelfke U 2003 Inclusion of stochastic organ movements in IMRT treatment planning *Radiother. Oncol.* **68** (Suppl. 1) S101–102

Unkelbach J and Oelfke U 2004a Organ movements in IMRT treatment planning: inverse planning based on probability distributions *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 104–7

Unkelbach J and Oelfke U 2004b Inclusion of organ movements in IMRT treatment planning via inverse planning based on probability distributions *Phys. Med. Biol.* **49** 4005–29

Unkelbach J and Oelfke U 2005 Incorporating organ movements in inverse planning: assessing dose uncertainties by Bayesian inference *Phys. Med. Biol.* **50** 121–39

Van den Heuvel F, Powell T, Seppi E, Littrupp P, Khan M, Wang Y and Forman J D 2003 Independent verification of ultrasound based image-guided radiation treatment, using electronic portal imaging and implanted gold markers, *Med. Phys.* **30** 2878–87

Van Herk M 2004 Errors and margins in radiotherapy *Semin. Radiat. Oncol.* **14** 52–64

Van Herk M, Scheider C, Sonke J J, Damen E and DeJaeger K 2002 Respiration-correlated CT of lung cancer patients *Radiother. Oncol.* **64** (Suppl. 1) S80–S81

Van Sörnsen de Koste, Lagerwaard F J, Nijssen-Visser M R J, Graveland W J and Senan S 2003 Tumor location cannot predict the mobility of lung tumours: a 3D analysis of data generated from multiple CT scans *Int. J. Radiat. Oncol. Biol. Phys.* **56** 348–54

Vedam S S, Keall P J, Docef A, Todor D A, Kini V R and Mohan R 2004 Predicting respiratory motion for four-dimensional radiotherapy *Med. Phys.* **31** 2274–83

Vedam S S, Keall P J, Kini V R and Mohan R 2001 Determining parameters for respiration-gated radiotherapy *Med. Phys.* **28** 2139–46

Vedam S, Keall P, Kini V, Motafavi H and Mohan R 2003b Predicting breathing motion for 4D radiotherapy (WIP) *Med. Phys.* **30** 1472

Vedam S S, Kini V R, Keall P J, Ramakrishnan V, Mostafavi H and Mohan R 2003a Quantifying the predictability of diaphragm motion during respiration with a non-invasive external marker *Med. Phys.* **30** 505–13

Verellen D, Linthout N and Storme G 2000 Comparison between different approaches for conformal treatment of the prostate: a theoretical and dosimetric evaluation *Proc. World Congress of Medical Physics and the AAPM Annual Congress (August 2000)* paper FR-EaBR-05

Visser A G, van Lin E N J T, Welmers A, Futterer J, Barentsz J O, van der Vight L P and van der Meazen R W M 2002 Fiducial markers for MRI-based target volume definition and treatment verification *Radiother. Oncol.* **64** (Suppl. 1) S41

Wagman R, Yorke E, Giraud P, Ford E, Sidhu K, Mageras G, Minsky B and Rosenzweig K 2001 Reproducibility of organ position with respiratory gating for liver tumors: use in dose-escalation *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 28

Webb S 1993 *The Physics of Three-dimensional Radiation Therapy—Conformal Radiotherapy, Radiosurgery and Treatment Planning* (Bristol: Institute of Physics Publishing)

Webb S 1997 *The Physics of Conformal Radiotherapy—Advances in Technology* (Bristol: Institute of Physics Publishing)

Webb S 2000 *Intensity Modulated Radiation Therapy* (Bristol: Institute of Physics Publishing)

Webb S 2004 *Contemporary IMRT—Developing Physics and Clinical Implementation* (Bristol: Institute of Physics Publishing)

Webb S 2005a The effect on IMRT conformality of elastic tissue movement and a practical suggestion for movement compensation via the modified dynamic multileaf collimator (dMLC) technique *Phys. Med. Biol.* **50** 1163–90

Webb S 2005b Limitations of a simple technique for movement compensation via movement-modified fluence profiles *Phys. Med. Biol.* **50** N155–N161

Webb S 2006a Does elastic tissue intrafraction motion with density changes forbid motion-compensated radiotherapy? *Phys. Med. Biol.* **51** 1449–62

Webb S 2006b Quantification of the fluence error in the motion-compensated dynamic MLC (DMLC) technique for delivering intensity-modulated radiotherapy (IMRT) *Phys. Med. Biol.* **51** L17–L21

Willoughby T R, Weinhous M S and Kupelian P A 2000 Daily transabdominal ultrasound localization of the prostate gland with the BAT system: 2705 alignments from 100 patients *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 308

Wilson E, Williams J, Lyn E and Aird E 2001 Active breathing control (ABC) in the treatment of non-small cell lung cancer (NSCLC) with chart week end less (CHARTWEL) *Radiother. Oncol.* **61** (Suppl. 1) S63

Wong J 2003 Methods to manage respiratory motion in radiation treatment *IMRT—the State of the Art: AAPM Medical Physics Monograph Number 29* ed J R Palta and T R Mackie (Madison, WI: Medical Physics Publishing) pp 663–702

Wu C, Jeraj R, Olivera G H and Mackie T R 2002 Re-optimization in adaptive radiotherapy *Phys. Med. Biol.* **47** 3181–95

Xing L, Crooks S, Li J G, Ozhasoglu C, Chen Y, Mehta V, Goffinet D, Beavis A and Boyer A 2000 Incorporating respiratory motion into the design of intensity maps in IMRT treatment of breast cancer *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 199

Xu B, Yan D, Kota K, Brabbins D S and Martinez A A 2000 The influence of inter and intra-patient rectum variation on treatment planning for prostate cancer radiotherapy *Proc. 42nd Annual ASTRO Meeting Int. J. Radiat. Oncol. Biol. Phys.* **48** (Suppl.) 191

Zhang G, Guerrero T, Huang T-C, Fitzpatrick M J, Ibbott G, Lin K-P and Starkschall G 2004a 3D optical flow method implementation for mapping of 3D anatomical structure contours across 4D CT data *Proc. 14th Conf. on the Use of Computers in Radiation Therapy (Seoul, Korea, May 2004)* pp 356–60

Zhang T, Keller H, O'Brien M J, Mackie T R and Paliwal B 2003 Application of the spirometer in respiratory gated radiotherapy *Med. Phys.* **30** 3165–71

Zygmanski P, Kung J H, Jiang S B, Choi N and Chen G 2001 Is IMRT of lung possible without respiratory gating? Clinical evaluation of a true dose received by a moving target volume *Int. J. Radiat. Oncol. Biol. Phys.* **51** (Suppl. 1) 27

Biography

Steve Webb has been Professor of Radiological Physics since 1996 and Head of the Joint Department of Physics of the ICR/RMH since 1998. He has PhD and DSc degrees and is a Fellow of the Institute of Physics (FInstP), the Institute of Physics and Engineering in Medicine (FIPEM) and the Royal Society (of) Arts (FRSA). He has published some 200 peer review papers in medical imaging and the physics of radiation therapy as well as five single-author textbooks and an 'edited by' in these areas. He was awarded the Silvanus Thompson medal of the British Institute of Radiology in 2004. He has been Visiting Professor at DKFZ Heidelberg, The University of Michigan at Ann Arbor, Memorial Sloan Kettering Cancer Centre New York and Harvard (Mass General Hospital, Boston). He is currently Editor in Chief of *Physics in Medicine and Biology.*