Journal of
Radiotherapy
in Practice

Journal of Radiotherapy in Practice 2004
4, 118–125

## Original Article

# A critical evaluation of internal organ immobilisation techniques

P. Bridge

*Faculty of Health and Wellbeing, Sheffield Hallam University, Sheffield, UK*

## Abstract

This paper aims to evaluate the range of techniques available to minimise both interfraction and intrafraction errors. The main interfraction errors are due to changes in volume of the rectum and bladder. Intrafraction errors are mainly due to respiration and to a lesser extent cardiac motion. There are various methods of minimising internal organ motion that attempt to permit reduction of the internal margin around the clinical target volume (CTV).

Techniques such as rectal balloon insertion and breathing control are evaluated to determine their role in reduction of margins for improved conformal radiotherapy. The paper concludes that rectal balloons have been shown to permit limited reduction of internal margins and morbidity levels. Breathing control has not increased reproducibility, but has allowed for reduction in lung morbidity. Reduction of margins can only be recommended when using breathing control in conjunction with daily CTV relocalisation.

Although these techniques do have a role to play at the moment, it appears that attempting to maintain a static environment within the highly mobile patient is fraught with difficulties and we must accept that there is always going to be motion. Rather than attempting to control the position of the tumour, future developments such as adaptive radiotherapy and tomotherapy may account for the movement.

**Keywords**

Immobilisation; internal organs; interfraction and intrafraction errors

## INTRODUCTION

The driving force behind improvements in radiotherapy is the improvement of the therapeutic ratio. The key to increasing this ratio is the use of conformal radiotherapy, using beam delivery innovations such as multileaf collimators (MLCs) and intensity modulated radiotherapy (IMRT) combined with improved tumour localisation with multiple imaging modalities. Most centres embarking on conformal radiotherapy have endeavoured to improve immobilisation techniques to ensure that the patient position is sufficiently reproducible to allow a decrease in the set-up margin. Geometrical errors from the machines, such as field size or measurement in angles can potentially be a source of error, although current manufacturer specifications mean that this is minimal.[1] Despite these improvements, there still remain considerable sources of uncertainty in CTV position that have the potential to render a conformal approach ineffective. There can be large variation in the relative position of internal anatomy on a daily basis. As Wu et al commented: "Prostate motion is the major source of error in radiation treatment delivery for prostate cancer."[2] [pp 69]

Increasing use of EPI systems to verify reproducibility can only ever provide reassurance that fields are in the same position with regards to skeletal anatomy as on localisation films. EPI's cannot demonstrate changes in position of soft tissue

---

Correspondence to: P. Bridge MSc, Faculty of Health and Wellbeing, Sheffield Hallam University, 11–15 Broomhall Road, Sheffield S10 2DR, UK. Tel: 0114 225 4336; Email: p.bridge@shu.ac.uk

CTV structures or take into account differences between the "snapshot" localisation position and daily treatment positions. For true improvements in therapeutic ratio to be gained from conformal radiotherapy, this uncertainty in CTV position needs to be reduced. If internal motion can be accurately measured, then an appropriate "internal" margin can be added onto the CTV.[3] Numerous studies have measured the errors associated with different tumour sites, as discussed by Langen and Jones in their excellent review article.[4] But for reduction in internal margin (and the associated dose escalation) it is not sufficient to measure the internal motion; it must be minimised.

The purpose of this paper is to describe briefly the sources of both interfraction and intrafraction errors and then evaluate the range of techniques available to minimise them. The implications of their use and their role in conformal radiotherapy will be assessed. The role of "external" patient immobilisation techniques will not be examined; although it must be stressed that "internal" immobilisation can only be made possible if used in conjunction with state-of-the-art daily patient position reproducibility.

## INTERFRACTION ERRORS

Uncertainty in CTV position on a daily basis is mainly due to variation in contents of the digestive and urinary systems. This variation can affect treatments to the bladder and digestive tract as well as adjacent structures such as the prostate and cervix.

### Bladder volume

It has long been accepted that bladder filling can have a significant effect on position of pelvic structures, which has led to some authors[5] recommending 2 cm margins for use with bladder boost treatments.

Numerous studies have researched the effect of bladder filling on reproducibility of adjacent organ position. In one typical study,[6] dual CT scans of 29 prone cervix/endometrium patients were performed to measure the effect of full and empty bladders on cervix position. The mean movements of the cervix due to bladder filling were found to be 7 mm cranially and 4 mm posteriorly, with minimal lateral movement.

There are a large number of studies[7–11] into uncertainty of prostate position, but few of these investigate the effect of bladder status alone. Studies investigating the effect of bladder variation on prostate motion are severely hampered by the much larger impact of variations in rectal volume, as will be discussed shortly. Adequate control of the rectal volume needs to be in place in order to determine the effect of bladder volume accurately.

Controversy surrounds the reported time-trend in bladder volume, with bladder size decreasing by up to 4% per week.[12] Antolak et al.[13] noted that there is a decrease in volume between the planning CT and the first fraction. Other authors[8] have disputed this and found an increase in bladder volume between planning and treatment due to possible retention or obstruction. They also found that bladder volume was constant throughout treatment, although this study did involve some control of rectal contents. These results suggest that variations in rectal volume can affect the bladder.

Despite this, personal experience has shown that bladder volume is much more routinely controlled than rectal volume. It is accepted that most departments will exert some degree of control over patient bladder status, although few will attempt to discuss rectal voiding.

### Rectal volume

Many studies have been performed to examine the variation of rectal volume and have demonstrated a reduction in volume of up to 6% per week.[12] Indeed, a recent study[14] confirmed that rectal volume is subject to a larger systematic error than random errors. Miralbell et al.[7] used weekly CT scans of prostate patients to determine that the ratio of treatment CTV: simulator CTV was 0.98 ± 0.11. Of further interest was the discovery that both rectum and bladder were similarly larger during treatment (ratios of 1.17 and 1.16 respectively), demonstrating a large systematic error. Of more relevance for this paper, however, was the increased variation in volume of the rectum (± 0.56) when compared to the bladder (± 0.25).

This further demonstrates the need for increased rectal volume control.

### Other sources

Other sources of interfraction errors are tumour or patient response, for example changes in patient contour or position[15] as radiotherapy progresses or shrinkage of the tumour[16]. These cannot be improved upon using immobilisation procedures, but require a commitment to adapt the treatment plan to the changing volume. This is beyond the scope of this paper.

## INTRAFRACTION ERRORS

If interfraction errors can be accounted for before each fraction, the tumour position during the fraction can be assumed to be constant. Intrafraction errors, however, offer no such guarantee due to the short timescale of the variations. Intrafraction errors are due mainly to the respiratory system and to a lesser extent to cardiac motion. Although this primarily affects thoracic treatments, the effect can also be transmitted along the body to the abdomen and pelvis.[17] The magnitude of intrafraction error in the thorax varies with position of the tumour from the lower lobe (5–22 mm) to the hilum (3–15 mm)[18]. The direction of motion is greatest in the superior-inferior direction (around 12 mm) with motion in other directions being around 2 mm.

The thorax is not the only tumour site affected by breathing. A study that generated fluoroscopic movies of gold markers demonstrated a link between prostate motion and breathing for different treatment positions.[17] It was found that prostate motion due to respiration was $<1$ mm when supine, but rose to 0.9–5.1 mm when prone. Another contributing factor to pelvic motion with breathing has been shown to be the use of thermoplastic shells.[19] In both cases, restriction of the abdominal motion has "internalised" the respiratory motion, causing rhythmic compression of the abdominal and pelvic organs.

A lesser factor causing intrafraction error is cardiac motion. Seppenwoolde[15] et al's correlation of lung tumour motion with cardiac frequency found that tumours close to the aorta experienced intrafraction motion from 1 to 4 mm induced by heartbeat. More distant tumours were not significantly affected.

## "INTERNAL" IMMOBILISATION TECHNIQUES

It can be seen that there are 3 main contributors to internal organ motion: bladder contents, rectal contents and respiratory motion. The remainder of this paper will evaluate the range of techniques and equipment available for immobilising these 3 main problem areas. Each problem will be addressed individually with a description and evaluation of relevant clinical results. The implications of the use of any equipment will be assessed in terms of patient comfort, time, cost and staff training issues.

### Bladder contents

The conventional method of encouraging patients to fill or void the bladder prior to treatment may not be effective at ensuring constant position of adjacent organs.[20] A study that used 80 cc of fluid in a urinary catheter balloon observed improved bladder immobilisation, but deemed reproducibility to be unsatisfactory.[5] This may be linked to patient discomfort or the relatively small volume of fluid in the balloon. Further studies into strict fluid control or increased volumes in a urinary balloon are indicated. As discussed previously, however, the effect of bladder volume variations is dwarfed by the effect of rectal fluctuations.

### Rectum contents

The simplest way to improve reproducibility in the pelvic region is to advise the patient to attend for radiotherapy with an empty rectum and encourage pre-treatment voiding. Stroom et al's[21] suggestion that laxatives can produce a more stable volume may be of value, but with diarrhoea being a major side effect of pelvic radiotherapy, medics may be reluctant to prescribe them. Even when empty, the position of the rectum can vary and cause interfraction errors. Rectal balloons containing a known volume of fluid or air can be used in conjunction with voiding or a laxative to stabilise rectal volume and position.

Most of the research into rectal balloon use has been concentrated on radiotherapy to the prostate. When the balloon is inflated here, it pins

***Table 1.*** *Typical prostate motion with rectal balloons*

| Authors | Number of patients | Air volume in balloon (cc) | SD AP (mm) | SD SI (mm) | SD LR (mm) |
|---|---|---|---|---|---|
| Teh et al.[23] | 10 | 100 | 1 | 1.78 | 1 |
| Patel et al.[22] | 5 | 60 | 2.6 | 3.1 | 1 |

the prostate against the pubic bone.[23] The volume of air used to inflate the balloon varies from 40 cc[24] to 100 cc.[23] Table 1 suggests how the reproducibility of prostate position may improve with increased balloon volume, although differences between the 2 studies inhibit a direct comparison. In fact, studies have yet to determine the optimal volume for improved reproducibility and minimum patient discomfort.[24] This may be due to the variation in rectal capacity between patients.

Wachter et al.[25] analysed CT scans at start and end of the course for 10 prostate patients to investigate the effect of rectal balloons on prostate position changes. They had empty bladders and rectal balloons were inserted. The study found 5 mm or more changes in the position of the post prostate border in 80% of patients with a deflated balloon and only 20% of patients with 40 cc of fluid in the balloon. Improvements such as this can allow for realistic reduction in margins for more conformal treatments.

The inflation of a rectal balloon has the added advantage of increasing the distance of the posterior rectal wall from the region of high dose. A prostate planning study determined that the mean ratio of the rectal high dose volume for an inflated balloon (60 cc) compared to a deflated one was 0.61 ($p = 0.01$).[22] This means that an inflated rectal balloon offered a sparing of 39% of high dose volume. This study was hampered by the use of a variety of external immobilisation positions with patients lying prone or supine, which may have introduced further errors.[26]

Teh et al.[23] assessed 116 patients' tolerance to rectal balloons containing 100 cc of air. 58.6% had "no problem", the rest reported it to be "uncomfortable but tolerable", although 2 patients had small build and requested a reduction in air volume to 50 cc. Good patient tolerance was also reported for a year's experience of routine rectal balloon use.[22] Some of these patients required topical ointment treatment, but all were able to use the balloon for the duration of the course.

The extra time needed for daily balloon placement has been estimated at 2–3 minutes per fraction.[22] Ultrasound checks to determine the positions of the prostate and balloon were also performed in this study, although it is not clear whether this was included within the extra time. Cost was minimised by wrapping each patient's balloon in a fresh disposable condom for each fraction.

Migration of the balloon superiorly in relation to the prostate throughout the radiotherapy course has been reported.[24] This implies poor reproducibility, but the authors did not position the balloon as strictly as other researchers and pulling the balloon till it rests on the sphincter may have minimised this effect.

## Respiration

Control of breathing is more problematic than maintaining constant rectal volume since the motion cannot be suspended completely and is continuous throughout the fraction. The internal immobilisation solutions are centred on either minimising the magnitude of the motion or gating.

An abdominal press has been utilised successfully to reduce lung tumour movement.[27] Patients experiencing over 5 mm movement under fluoroscopy had abdominal pressure applied. The daily set-up errors were reduced to less than 5 mm. Patient comfort was not reported in this study, but some compromise could be expected if breathing is forcibly restricted using external pressure.

A more elegant approach to reducing intrafraction errors due to respiration is gating. Breathing is monitored such that radiation can be delivered at a consistent point in the breathing cycle. The efficacy of this technique can be improved by encouraging breath-holding and increasing the dose rate to maximise the short irradiation times.

Respiration can be monitored in a variety of ways. Temperature sensors or a spirometer can measure the airflow. Other authors have utilised a strain gauge around the torso,[28] an LED displacement monitor[29] or video cameras[30] to measure the respiratory cycle. Techniques can be taught to the patient to enable them to maintain breath holds for 12–16 seconds.[30] This allows the treatment to be delivered in typically 1 or 2 breath holds per field. Kim et al.[30] successfully allowed the patient to gate the treatment themselves with an interlock switch. A high degree of patient compliance is essential for this to be successful, and most authors prefer to retain control of the irradiation.

The potential benefits of controlling respiration were neatly demonstrated by a study that triple-planned patients.[31] Plans were generated for free-breathing (with normal 1 cm margin), deep inspiration hold (normal 1 cm margin) and deep inspiration hold (margins determined by fluoroscopy). There was a mean reduction of 33% in the percentage of lung volume receiving 20 Gy, offering a significant reduction in morbidity.

Patient discomfort is not compromised with these techniques since the patient judges how long they can hold a breath for. Poor patient compliance can produce variations due to different positions of breath-hold, air leakage, COPD and variation in exhalation effort. The ABC system, as described by Wong et al.[32] was designed to address these problems.

Several authors have studied the effect of ABC on the volume of lung in the high dose region. Cheung et al.[33] took daily CT scans of peripheral non-small cell lung tumours over a 5-day period with and without ABC at maximum inspiration. Inspiration breath hold could potentially increase the total lung volume and hence decrease the percentage of lung in the treated volume. This depends on the site of the tumour as suggested by Remouchamps.[34] The study found that ABC reduced the volume of lung in the PTV by 18% and the volume receiving the critical 20 Gy dose by 13% ($p = 0.002$). Interestingly, the authors did not recommend reducing the 1.5 cm margin as one might expect the ABC apparatus to allow, instead noting considerable variation in position.

Reproducibility of lung volume is also desirable in other tumour sites. Moderate deep inspiration (75% of maximum) breathing control was evaluated with 30 patients receiving radiotherapy to the left breast.[34] Conversely to Cheung et al, the authors concluded that they could reduce the internal margins to 3–4 mm (when analysing motion of the upper 2/3 of the lungs) and 6–7 mm (lower 1/3). A more recent study evaluated the potential role of ABC for improving delivery of IMRT to the breast.[35] The study concluded that ABC did not make a noticeable improvement in breast dose although, as the authors postulated, irradiating at deep inspiration would have the added benefit of increasing the distance from the heart to the chest wall.

The liver is another site where respiratory motion can affect tumour motion. ABC has been shown to produce less than 1 mm of movement of liver tumours compared to 4 mm movement with free breathing.[32] This excellent intrafraction reproducibility was confirmed by a fluoroscopic study.[17] Unfortunately this study also highlighted considerable interfraction variability, with a mean standard deviation of 4.3 mm cranio-caudally. This implies that the apparatus can immobilise the breathing cycle at the same point during a fraction, but the point at which it can do this varies on a day-to-day basis. This may be because it does not rely on an accurate measurement to determine the breath hold position, but rather depends on a comparison to the end of normal expiration. This variability means that margins cannot be reduced. The intrafraction error can be reduced, but an underlying interfraction error has been discovered. The authors of this study recommended PTV shrinkage ONLY in conjunction with daily relocalisation.

This finding is common to many studies into ABC and may be one of its limitations. One study reported sufficient confidence in a voluntary breath-holding technique to decrease margins and increase dose from 69.4 Gy to 87.9 Gy.[36] This study relied on weekly portal films to ensure reproducibility, however, which may have induced false confidence. More recent studies have demonstrated that internal positioning errors are still occurring. It can be seen, then, that the ABC equipment can reduce the volume of lung receiving a high dose, but cannot allow a reduction in margins and escalation of dose. While this is good news in terms of pulmonary morbidity, the anticipated improvements in conformality and dose escalation have not been made possible.

Few studies have rigorously investigated patient comfort, although high compliance levels have been noted.[33] Patients have reported a dry mouth during the treatment, but this would not be anticipated as a problem over the duration of a normal treatment session.

## THE ROLE OF INTERNAL ORGAN IMMOBILISATION

It has been seen that internal organ immobilisation can provide significant improvements to morbidity of rectal walls and normal lung tissues. Reductions in internal margins have been shown to be possible by some authors using rectal balloons. This may not be the only solution to the problem, however. Few centres require their patients to follow strict control over their rectal contents, possibly due to an unwillingness to broach the subject. It may be of use to compare strict regulation of patient diet and voiding patterns with rectal balloons to determine the need for this equipment. Balloons would appear to have a useful role to play, but it may be that improved control of rectal status at time of treatment would have a similar effect on immobilisation. This would, of course, not provide the decrease in rectal dose, but would not involve an invasive and potentially time-consuming procedure.

When evaluating reduction of respiratory motion, the immobilisation afforded by breathing control techniques does not translate to a reduction in margins and subsequent dose escalation. The benefits afforded by this equipment are more associated with reduced morbidity, rather than enhancing tumour control. Breathing control devices have a definite role to play in the reduction of intrafraction errors but cannot eradicate interfraction errors. The majority of studies reviewed for this paper suggest that the future role of breathing control devices could be in conjunction with daily online localisation with fluoroscopy or MVCT. Daily relocalisation could locate the point in the breathing cycle to initiate irradiation and breathing control devices could ensure that irradiation only occurs at that point.

It has also been demonstrated that patient tolerance of "internal immobilisation" techniques is generally acceptable, although there is a scarcity of studies that attempt a thorough evaluation of the patient experience. Although some measures such as control of bladder contents or voluntary breath-holding have no impact on patient comfort, this may not be true of the more invasive procedures. Rectal balloon insertion and forced breathing cessation conjure up images more akin to a torture chamber than a treatment room. Patient tolerance of procedures is, of course, linked with perceived benefit but a more formal investigation of patient feelings would be useful prior to more widespread implementation of these techniques.

A factor that may be inhibiting more widespread usage of "internal immobilisation" is the time-consuming nature of the treatments. This is especially true of the complicated breathing control techniques. Even the voluntary breath-hold technique is associated with an increase in treatment time from 17 minutes to 33 minutes,[36] mainly due to the inclusion of daily patient coaching. The ABC system requires a preliminary coaching session, but claims a shorter treatment time. Authors quote favourable comparisons with normal techniques, such as 20 minutes,[33] but it is anticipated that outside the constraints of a trial, with a wider group of patients and the pressures of increasing waiting lists, this time could become a deciding factor in prioritising use of this apparatus.

Another issue surrounding internal immobilisation techniques is the need for specialised radiographer training. Insertion of rectal balloons and use of ABC apparatus should only be undertaken by trained personnel. Balloon insertion should be able to be performed by therapy radiographers, since diagnostic radiographers now perform the similar enema procedure.

## CONCLUSION

It can be seen that internal immobilisation has a potential role to play, but studies have yet to prove that these improvements are not made at the expense of patient comfort and throughput. Pelvic organ immobilisation techniques are providing real reductions in margins. For sites affected by breathing motion, however, the expected benefits of reduced margins are not being delivered. The improvement afforded by gating can only translate to a reduction in margin if daily relocalisation is performed.

Future developments may mean that these techniques may not be necessary. Instead of attempting to maintain a static environment within the highly mobile patient, we must accept that there is going to be motion. Rather than attempting to control the position of the tumour, the treatment could take into account the movement. Daily CT scanning[37], cone beam CT,[38] tomotherapy[39] or seed implant imaging[11] are currently being evaluated as methods of localising or tracking tumour position. Once accurate relocalisation information is obtained, adaptive processes can be applied to treatment, leading to a reduction in margins and escalation of dose.[40] This process can take place retrospectively, but it is feasible that a tumour undergoing intrafraction motion could be tracked and irradiated while it moves, rather than "merely" gating the treatment. The technology exists to deliver dynamic radiotherapy and currently that is being used to enhance a static dose distribution. If tumour position can be accurately localised during treatment, true dynamic radiotherapy could be used to target the tumour and deliver the required dose distribution wherever the tumour happens to be within the patient.

## References

1. Stroom JC, Heijmen BJM. Geometrical uncertainties, radiotherapy planning margins, and the ICRU-62 report. Radiother Oncol 2002; 64: 75–83.
2. Wu J, Haycocks T, Alasti H, Ottewell G, Middlemiss N, Abdolell M, Warde P, Toi A, Catton C. Errors from field placement and organ motion during conformal radiotherapy for prostate cancer. Journal of Radiotherapy in Practice 2001; 2: 65–73.
3. International Commission on Radiation Units and Measurements. ICRU Report 62. Prescribing, recording, and reporting photon beam therapy (Supplement to ICRU Report 50). Bethesda: ICRU, 1999.
4. Langen KM, Jones DTL. Organ motion and its management. Int J Rad Oncol Biol Phys 2001; 50: 265–278.
5. Miralbell R, Nouet P, Rouzaud M, Bardina A, Hejira N, Schneider D. Radiotherapy of bladder cancer: relevance of bladder volume changes in planning boost treatment. Int J Radiat Onc Biol Phys 1998; 41: 741–746.
6. Buchali A, Koswig S, Dinges S, Rosenthal P, Salk J, Lackner G, Böhmer D, Schlenger L, Budach V. Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer. Radiother Oncol 1999; 52: 29–34.
7. Miralbell R, Ozsoy O, Pugliesi A, Carballo N, Arnalte R, Escude L, Jargy C, Nouet P, Rouzard M. Dosimetric implications of changes in patient repositioning and organ motion in conformal radiotherapy for prostate cancer. Radiother Oncol 2003; 66: 197–202.
8. Mechalakos JG, Mageras GS, Zelefsky MJ, Lyass O, van-Herk M, Kooy HM, Leibel SA, Ling CC. Time trends in organ position and volume in patients receiving prostate three-dimensional conformal radiotherapy. Radiother Oncol 2002; 62: 261–265.
9. Little DJ, Dong L, Levy LB, Chandra A, Kuban DA. Use of portal images and BAT ultrasonography to measure setup error and organ motion for prostate IMRT: implications for treatment margins. Int J Rad Oncol Biol Phys 2003; 56: 1218–1224.
10. Lock M, Wong E, Paradis E, Moiseenko V, Rodrigues G, D'Souza D, Kron T, Venkatesan V, Downey D, Ash R, Bauman G. Impact of urethrography on geometric uncertainty in prostate cancer radiotherapy. Int J Rad Oncol Biol Phys 2003; 57: S331–S332.
11. Kitamura K, Shirato H, Seppenwoolde Y, Onimaru R, Oda M, Fujita K, Shimizu S, Shinohara N, Harabayashi T, Miyasaka K. Three-dimensional intrafractional movement of prostate measured during real-time tumor-tracking radiotherapy in supine and prone treatment positions. Int J Rad Oncol Biol Phys 2002; 53: 1117–1123.
12. Lebesque JV, Bruce AM, A. P. Guus Kroes, Adriaan Touw, Tarek Shouman and Marcel van Herk Variation in volumes, dose-volume histograms, and estimated normal tissue complication probabilities of rectum and bladder during conformal radiotherapy of T3 prostate cancer. Int J Rad Oncol Biol Phys 1995; 33: 1109–1119.
13. Antolak JA, Rosen II, Childress CH, Zagars GK, Pollack A. Prostate target volume variations during a course of radiotherapy. Int J Rad Oncol Biol Phys 1998; 42: 661–672.
14. Hoogeman MS, van Herk M, de Bois J, Muller-Timmermans P, Koper PCM, Lebesque JV. Quantification of local rectal wall displacements by virtual rectum unfolding. Radiother Oncol 2004; 70: 21–30.
15. Seppenwoolde Y, Shirato H, Kitamura K, Shimizu S, van Herk M, Lebesque JV, Miyasaka K. Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat, measured during radiotherapy. Int J Rad Oncol Biol Phys 2002; 53: 822–834.
16. Roeske JC, Forman JD, Mesina CF, He T, Pelizzari CA, Fontenla E, Vijayakumar S, Chen GTY Evaluation of changes in the size and location of the prostate, seminal vesicles, bladder, and rectum during a course of external beam radiation therapy. Int J Rad Oncol Biol Phys 1995; 33: 1321–1329.
17. Dawson LA, Brock KK, Kazanjian S, Fitch D, McGinn CJ, Lawrence TS, Ten Haken RK, Balter J. The reproducibility of organ position using active breathing control (ABC)

during liver radiotherapy. Int J Radiat Onc Biol Phys 2001; 51: 1410–1421.

18. Ross CS, Hussey DH, Pennington EC. Analysis of movement of intrathoracic neoplasms using ultrafast computerized tomography. Int J Radiat Oncol Biol Phys 1990; 18:671–677.
19. Malone S, Crook JM, Kendal WS, Zanto JS. Respiratory-induced prostate motion: quantification and characterization. Int J Radiat Onc Biol Phys 2000; 48: 105–109.
20. Muren LP, Smaaland R, Dahl O. Organ motion, set-up variation and treatment margins in radical radiotherapy of urinary bladder cancer. Radiother Oncol 2003; 69: 291–304.
21. Stroom JC, Koper PCM, Korevaaar GA, Van Os M, Janssen M, De Boer HCJ, Levendag PC, Heijmen BJM. Internal organ motion in prostate cancer patients treated in prone and supine treatment position. Radiother Oncol 1999; 51: 237–248.
22. Patel RR, Orton N, Tomé WA, Chappell R, Ritter MA. Rectal dose sparing with a balloon catheter and ultrasound localization in conformal radiation therapy for prostate cancer. Radiother Oncol 2003; 67: 285–294.
23. Teh BS, Woo SY, Mai W, Mcgary JE, Carpenter LS, Lu HH, Chiu JK, Vlachaki MT, Grant WH, Butler EB. Clinical experience with intensity-modulated radiation therapy (IMRT) for prostate cancer with the use of rectal balloon for prostate immobilization. Medical Dosimetry 2002; 27: 105–113.
24. Ciernik IF, Baumert BG, Egli P, Glanzmann C, Lütolf UM. On-line correction of beam portals in the treatment of prostate cancer using an endorectal balloon device. Radiother Oncol 2002; 65: 39–45.
25. Wachter S, Gerstner N, Dorner D, Goldner G, Colotto A, Wambersie A, Pötter R. The influence of a rectal balloon tube as internal immobilization device on variations of volumes and dose-volume histograms during treatment course of conformal radiotherapy for prostate cancer. Int J Radiat Onc Biol Phys 2002; 52: 91–100.
26. Bayley AJ, Catton CN, Haycocks T, Kelly V, Alasti H, Bristow R, Catton P, Crook J, Gospodarowicz MK, McLean M. A randomized trial of supine vs. prone positioning in patients undergoing escalated dose conformal radiotherapy for prostate cancer. Radiother Oncol 2004; 70: 37–44.
27. Negoro Y, Nagata Y, Aoki T, Mizowaki T, Araki N, Takayama K, Kokubo M, Yano S, Koga S, Sasai K. The effectiveness of an immobilization device in conformal radiotherapy for lung tumor: reduction of respiratory tumor movement and evaluation of the daily setup accuracy. Int J Radiat Onc Biol Phys 2001; 50: 889–898.
28. Kubo HD, Hill BC. Respiration gated radiotherapy treatment: A technical study. Phys Med Biol 1996; 41: 83–91.
29. Minohara S, Kanai T, Endo M. Respiratory gated irradiation system for heavy-ion radiotherapy. Int J Radiat Oncol Biol Phys 2000; 47: 1097–1103.
30. Kim DJ, Murray BR, Halperin R, Roa WH. Held-breath self-gating technique for radiotherapy of non-small-cell lung cancer: a feasibility study. Int J Radiat Oncol Biol Phys 2001; 49: 43–49.
31. Barnes EA, Murray BR, Robinson DM, Underwood LJ, Hanson J, Roa WHY. Dosimetric evaluation of lung tumor immobilization using breath hold at deep inspiration. Intl J Radiat Onc Biol Phys 2001; 50: 1091–1098.
32. Wong JW, Sharpe MB, Jaffray DA, Kini VR, Robertson JM, Stromberg JS, Martinez AA. The use of active breathing control (ABC) to reduce margin for breathing motion. Int J Radiat Onc Biol Phys 1999; 44: 911–919.
33. Cheung PCF, Sixel KE, Tirona R, Ung YC. Reproducibility of lung tumor position and reduction of lung mass within the planning target volume using active breathing control (ABC). Int J Radiat Onc Biol Phys 2003; 57: 1437–1442.
34. Remouchamps VM, Letts N, Yan D, Vicini FA, Moreau M, Zielinski JA, Liang J, Kestin LL, Martinez AA, Wong JW. Three-dimensional evaluation of intra- and interfraction immobilization of lung and chest wall using active breathing control: A reproducibility study with breast cancer patients. Int J Radiat Onc Biol Phys 2003; 57: 968–978.
35. Frazier RC, Vicini FA, Sharpe MB, Yan D, Fayad J, Baglan KL, Kestin LL, Remouchamps VM, Martinez AA, Wong JW. Impact of breathing motion on whole breast radiotherapy: a dosimetric analysis using active breathing control. Int J Radiat Onc Biol Phys 2004; 58: 1041–1047.
36. Rosenzweig KE, Hanley J, Mah D, Mageras G, Hunt M, Toner S, Burman C, Ling CC, Mychalczak B, Fuks Z, Leibel SA. The deep inspiration breath-hold technique in the treatment of inoperable non-small-cell lung cancer. Int J Radiat Oncol Biol Phys 2000; 48: 81–87.
37. Kuriyama K, Onishi H, Sano N, Komiyama T, Aikawa Y, Tateda Y, Araki T, Uematsu M. A new irradiation unit constructed of self-moving gantry-CT and linac. Int J Radiat Onc Biol Phys 2003; 55: 428–435.
38. Sidhu K, Ford EC, Spirou S, Yorke E, Chang J, Mueller K, Todor D, Rosenzweig K, Mageras G, Chui C. Optimization of conformal thoracic radiotherapy using cone-beam CT imaging for treatment verification. Int J Radiat Onc Biol Phys 2003; 55: 757–767.
39. Mackie TR, Kapatoes J, Ruchala K, Lu W, Wu C, Olivera G, Forrest L, Tome W, Welsh J, Jeraj Rl. Image guidance for precise conformal radiotherapy. Int J Radiat Onc Biol Phys 2003; 56: 89–105.
40. Martinez AA, Yan D, Lockman D, Brabbins D, Kota K, Sharpe M, Jaffray DA, Vicini F, Wong J. 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 Onc Biol Phys 2001; 50: 1226–1234.