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Feasibility of the use of the Active Breathing Coordinator™ (ABC) in patients receiving radical radiotherapy for Non Small Cell Lung Cancer (NSCLC)

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Abstract

Introduction

Lung tumour movement is one of the major challenges in radiotherapy. A patient's breathing pattern does not only vary between breath holds but also daily. The range of motion has been found to be as much as 12mm +/- 6mm in lower lobe tumours {Seppenwoolde, 2002 1 /id}. As a consequence planning target volume (PTV) margins in the region of 1.5-2cm are used when treating patients with radical radiotherapy. There are varying technical approaches being investigated to compensate for tumour motion and hence reduce margins. Tracking the tumour is one and involves the use of implanted markers which is an invasive procedure {Shimizu, 2001 16 /id}. Another method is to synchronise the treatment delivery with tumour movement ('gate' the treatment) using external markers to monitor respiration and the information fed back to the linac {Ford, 2002 12 /id; Shirato, 2000 21 /id}. However to be effective, the relationship between the external marker movement and tumour position must be constant. Erratic breathing patterns affect the reproducibility {Ford, 2002 12 /id; Mageras, 2001 15 /id} although the use of audio
breathing instructions and visual aids have been found to make breathing more regular {Kini, 2003 24 /id; Vedam, 2001 26 /id; George 2006}. The use of 4d CT has been proposed to determine the tumour mean position and create an internal target volume {Wolthaus, 2008 57 /id}. However this requires 4D equipment to be available at planning and treatment for verification. Rather than compensating for the motion an alternative approach is to reduce motion. Voluntary breath hold or assisted breath hold using a breathing control device (Active Breathing Coordinator™, ABC) can be used to maintain a constant tumour position between planning and treatment {Rosenzweig, 2000 22 /id; Wong, 1999 15 /id}. However, is again important that the inter-fraction and intra-fraction reproducibility of the breath holds are established {Cheung, 2003 14 /id; Wilson, 2003 3 /id}. In addition it has been speculated that the use of ABC during radical for lung cancer would be too demanding for patients (Kimura 2004, Kashani 2006, Rosenzweig 2000).

We have found in a previous study that lung cancer patients can maintain an average breath hold time of 20 seconds {Panakis, 2008 100 /id}. This study aims to test the feasibility of treating patients with radical radiotherapy using ABC.

Methods

The study protocol was approved by the local Committee for Clinical Research (CCR) and Local Research Ethics Committee (REC). Eighteen patients referred for radical radiotherapy for non small cell lung cancer (NSCLC) were consented for treatment using ABC. The equipment consists of a

Patient training

Patients were trained immediately prior to the planning CT scan. Initially they were shown how to correctly position the mouthpiece between their teeth and lips and the importance of maintaining a good seal with their lips was emphasised. After which they assumed the treatment position, on an in-house developed lung board, the mouthpieces and nose clip attached and allowed to breathe gently until they felt comfortable i.e when the breathing trace on the ABC screen was regular. They were then asked to perform repeated deep breaths with gentle breaths in between and the maximum inspiratory volume (MIV) was recorded. The breath hold volume for treatment
(threshold level) was initially set at 70% of the maximum inspiratory volume and a 5 second breath hold time was entered. The patient was asked to take a deep breath and assisted breath hold commenced when the breathing trace crossed the threshold volume level. The seconds remaining during breath hold was counted down by the radiographer controlling the device via the room microphones and a radiographer remained with the patient to reassure and check comfort. The breath holds were increased in 5 second intervals only when the patient was comfortable. The maximum breath hold time and the threshold level were saved in the patient file.

**CT planning**

When maximum breath hold time was reached a contrast scan without the ABC device, free breathing (FB), was acquired (Philips Brilliance CT Big Bore, Philips Medical Systems UK) using 2mm slice thickness. The tattoo positions were marked in free breathing. A surview was then acquired with ABC to plan the scan using a fast protocol i.e rotation time decreased from 0.75 secs to 0.5 secs and the pitch increased from 0.3 to 0.7. Although the increased pitch would reduce resolution the breath hold would increase resolution by eliminating blurring due to breathing. An extra 5 seconds was added onto the scan time indicated from the scanner to determine the breath hold time required for the scan to be captured in a single breath hold. If this was not possible then a split scan was performed.

A 3-field coplanar conformal plan treating patients to a dose of 64Gy in 32 fractions was produced for each scan using Pinnacle³. The simulator was used to verify the isocentre in breath hold using digitally reconstructed radiographs (DRR’s) imported into Omnipro (…………..). This also re- familiarised the patients with the ABC procedure before treatment commenced.

**Treatment**

Patients were treated on Elekta linear accelerators (Elekta Oncology Systems Ltd Crawley, West Sussex, England) with iview electronic portal imaging (EPI) system. The patient was aligned to the tattoos in free breathing. The isocentre from the ABC plan was set in the anterior-posterior
(AP) direction using the couch height, correcting for couch sag. In the right-left (RL) and superior-inferior (SI) directions the isocentre was initially set to the anterior tattoo in breath hold. The couch position was noted and the required distance to the planned isocentre moved using the couch read out which allowed the patient to breath freely during this time.

Audio instructions were used from outside the room to instruct the patient for breath hold. The patient was prompted at peak of a cycle to ‘breathe gently and then when you are ready take a deep breath in’. The linac was switched on at the trough of the breath prior to the hold to compensate for the time delay (Fig 1). The maximum breath hold time was used and a radiographer counted the seconds down using the audio system. The linac and ABC interface were not connected which meant when either the treatment beam or the breath hold had completed the breath hold or linac was manually interrupted. Also when the beam was interrupted by the automatic wedge the linac was manually interrupted and the ABC deactivated. Once the wedge was in place the patient prompted and the beam restarted as above.

Orthogonal EPI were taken to evaluate any treatment set-up displacement. A no action level (NAL) protocol was used, on the first three fractions EPI’s were averaged to calculate the systematic errors and this was corrected for on fraction four. EPIs were repeated weekly and a tolerance of 6 mm used. The set up displacement, with and without correction applied, was used to calculate the systematic error ($\Sigma$) of the group, the standard deviation (SD) of the distribution of the average set-up displacements per patient and the random error ($\sigma$) of the group, the SD of the patients set-up displacements averaged over the patient group. During treatment the total treatment time (patient on and off the bed) and number and length of breath holds required were recorded. Patients were asked to fill in a questionnaire weekly and rate how uncomfortable they found the device, choosing from Not at all, A little, Quite a bit, or Very much. There was also free text space for comments.

To assess reproducibility of tumour position during radiotherapy two further CT scans using the ABC device were acquired in the middle (ABCmid) and at the end of the treatment schedule (ABCend).
Staff training

Training sessions were conducted with the staff prior to use. This included an overview of the system and practicing activating the ABC device whilst giving audio prompts. Consistent audio instructions were recommended to avoid misinterpretation by the patient and aid communication between the ABC operator and linac operator. Both systems had to be activated independently as gating was not available.

Quality assurance of ABC

Two ABC devices were used, CT and treatment. It was essential that breath hold volumes for predetermined threshold levels were consistent within and compared to each device. A calibration system was devised using a 3 litre volumetric syringe (Hans Rudolph Model 5530) and an in house developed ABC volume curve analysis software. The ABC turbine and valve were coupled directly to the syringe and the laptop computer connected directly to the ABC control unit. Repeated syringed ‘breath’ holds using a threshold of 1 litre were performed and the volume of the syringe plunger position was measured using a scaled ruler with 0.01 litre increments. The software analysed volume curves to give statistical data for each breath and generated a chart for analysis. The statistics for held breaths were: the threshold volume (Vt), the start and stop times of the hold and the flow averaged over the first 100ms of the hold period (Fh). This software was also used to analyse the patients breath holds during treatment sessions.

Results

Feasibility

17 patients completed 32 fractions radiotherapy. 1 patient (patient 13) requested to be treated without the device after 2 weeks of treatment. The mean (SD) patient training time was 13.8(4.8)mins.

All patients tolerated a maximum breath hold time of >15 seconds and the mean (SD) was 20 (3.5) secs. There was no correlation between maximum breath hold time and age, FEV1 or performance status. The range of ages and breath hold times is illustrated in Figure 2.
The mean (SD) threshold level was 1.33(0.38) litres held at a mean (SD) of 69 (13)% of the MIV. The mean (SD) breath hold time per patient per session was between 10.3(7.6) secs and 14.6(2.4) secs with a mean of between 6 -13 breath holds.

**CT planning**

All planning scans were acquired in a single breath hold. Although the increased pitch would reduce resolution, the breath hold increased resolution by eliminating blurring due to breathing and resulted in a good quality CT scan. Figure 3 shows a comparison of ABC and free breathing scan.

Add – Comparison of ABC breath hold recorded compared to actual lung volume measured on CT. Variations

**Treatment**

The mean (SD) treatment time (patient on – off the bed) was 15.8(5.8) mins.

Questionnaires of 15 patients were collected (3 were misplaced). No patient found the ABC very uncomfortable (Figure 2). 2 patients (patient 3 and patient 7) found the device ‘Quite a bit uncomfortable’ at CT planning but this deceased to ‘A little’ by week 2 for patient 7 and by week 3 for patient 3. In only 1 patient (patient 15) the level of discomfort increased during treatment because of a cold (week 3). This resolved in week 4 and the level of discomfort decreased again. It is interesting to note that patient 13 who requested to be treated without ABC had recorded the device as only ‘A little’ uncomfortable.

The problems patients recorded included problems with the nose piece (2 patients), dry mouth (2 patients), coughing (1 patient). 6 patients made positive comments regarding how staff encouraged and helped them relax.

The mean breath hold volumes per patient as recorded by ABC ranged between 1.08 litres and 2.66 litres with a range of SD between 0.03 litres and 0.12 litres. Flow breath hold, Variability

**Set-up accuracy**
Using the NAL protocol the $\Sigma$ was reduced to <2mm in the right-left (RL) and the anterior-posterior (AP) direction (Table 2). A $\Sigma$ of 2.4mm remained in the superior-inferior direction which was also the direction where the largest random error was determined.

**Quality Assurance**

Calibration of devices showed a reaction time of …..and …….ms of ABC CT and ABC treatment respectively. The breath hold is related to speed of flow at threshold level (Figure 2). was…….. and

**Discussion**

This is the first study reporting the feasibility of the treatment of lung cancer patients using ABC. Seventeen out of 18 patients completed a radical course of radiotherapy using ABC. The mean breath hold time of 20 secs determined here was comparable with our previous study {Panakis, 2008 100 /id} and other studies where the feasibility of ABC was evaluated without treating patients with ABC {Wilson, 2003 3 /id; Wong, 1999 15 /id; Koshani, 2006 16 /id}. The acceptability rate with ABC is better compared to studies using deep inspiration breath hold (dIBH) possibly due to the fact that ABC uses 70%-80% of MIV whereas dIBH used 100% vital capacity which may have caused fatigue {Rosenzweig, 2000 22 /id}. However it was not necessary to continually use the maximum breath hold volume during treatment and we have since implemented ABC for all NSCLC patients receiving radiotherapy and recommend a minimum maximum breath hold time of 15 seconds.

Although exhale has been shown to hold the tumour in a more reproducible position than inhale {Koshani, 2006 16 /id} we used mid deep inspiration (mDIBH) breath hold. Not only is it more natural to breath hold after inhalation, it also allows the potential advantage of treating patients with inflated lungs, increased lung volume and lower lung density, to be utilized and enable dose escalation {Hanley, 1999 17 /id}. This has been investigated in this group of patients and published in a separate report (Partridge in press 2009).
The evolution of CT scanners enabled helical scanning and a fast protocol to be used which eliminated the need for more than 1 scan to cover the entire thorax as described earlier reports (Cheung, 2003 14 /id; Koshani, 2006 16 /id; Remouchamps, 2003 4 /id; Wilson, 2003 3 /id; Wong, 1999 15 /id). Although there is a risk of losing resolution by using a fast scan the benefit of ABC, reduction of blurring caused by breathing, counteracted this.

Coaching for gating has found that a combination of audio and visual aids improve the reproducibility of breathing cycles; audio aid improved frequency and visual aid improved the amplitude (George). With ABC we found audio coaching only adequate and a visual aid was not beneficial possibly because the threshold volume for breath hold is pre determined at the training session hence patients are not ‘aiming’ for a specific breath volume. Cheung suggests that patients need to be coached to breathe evenly and consistently to ensure the volume is consistent because the ABC resets expiration at baseline hence the volume and potentially the tumour position may be different in each breath hold (Cheung, 2003 14 /id). However Cheung used comfortable inspiration which may be more difficult to reproduce. We used mDIBH and found that the median of the patients mean flow rate was 1.04 l/s (range 0.59 – 2.05 l/s) with a median SD of 0.21 l/s (0.12-0.4 l/s). The threshold and held volume difference ranged between Remouchamps found that with a flow rate of 2 l/s there was a 300ml overshoot for 1.8 L inspired volume. This was reduced for a rate of 1 l/s (Remouchamps, 2003 50 /id).

Discuss variability of ABC and relation to flow rate at breath hold Then variability of ABC recorded volume translated into …cc actual held volume at CT. Point- although the ABC overshoot resulted variability of breath hold it did not translate into a large variability in lung volume ….Suggest a limit for accuracy

Staff training is important because if the staff are confident it may help the patient relax. 6 patients made positive comments regarding the instructions given by the radiographers. The importance of clear communication has been emphasised in earlier studies where poor communication has
previously been cited as a reason for patients not tolerating ABC {Rosenzweig, 2000 13 /id ; Eccles, 2006 18 /id}.

EPI images and bony anatomy were used to evaluate set up displacements and although the $\Sigma$ and $\sigma$ errors found here agreed with other published reports EPI has been shown to be less accurate than 3d kilo-voltage imaging, cone beam CT (CBCT) {Borst, 2007 30 /id}. This was due to the poor image quality of EPI in the thorax region. Using the diaphragm as a surrogate of tumour position may seem logical, particularly since the patient is in breath hold. However this was shown not to be accurate (Brock). It takes 2 mins to acquire a CBCT image which is too long for a single breath hold and currently it is not possible to interrupt the CBCT acquisition. Until the technology improves it is not possible to use CBCT with ABC.

Conclusions
The use of ABC in patients receiving radical radiotherapy for NSCLC is feasible. A minimum breath hold time of 15 secs is recommended prior to commencing treatment. The development of gating the ABC with the linac and the development of CBCT software would improve the treatment delivery and verification.
Figure 1. Schematic diagram showing breathing cycle, when to prompt the patient to take a deep breath and the breath hold.

1 = prompt patient to ‘take a gentle breath and then a deep breath’
2 = Linac switched on
3 = Breathing trace crosses threshold, balloon valve closes and patient begins breath hold
Figure 2. Age, breath hold time and performance status of patients treated with ABC
Figure 3a. CT scan acquired with patient in Free Breathing (FB)
Figure 3b. CT scan acquired with patient using Active Breathing Coordinator (ABC)
Figure 4. Response from patient questionnaire. How uncomfortable did you find the device?

Where: 1 = Not at all; 2 = A little; 3 = Very much; 4 = Quite a bit
Table 1. Set-up errors calculated without (i.e. aligning to skin marks only) and with the no action level protocol applied

<table>
<thead>
<tr>
<th>Set up protocol</th>
<th>Right-left (mm)</th>
<th>Superior-Inferior (mm)</th>
<th>Anterior-posterior (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>∑</td>
<td>Skin marks</td>
<td>2.9</td>
<td>3.9</td>
</tr>
<tr>
<td>σ</td>
<td>Skin marks</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>∑</td>
<td>No action level protocol</td>
<td>1.9</td>
<td>2.4</td>
</tr>
<tr>
<td>σ</td>
<td>No action level protocol</td>
<td>3</td>
<td>3.7</td>
</tr>
</tbody>
</table>

∑ - Systematic error
σ - Random error