**Incidence and evolution of imaging changes on cone-beam CT during and after radical radiotherapy for non-small cell lung cancer**

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**Abstract**

*Background and purpose*

Cone beam CT (CBCT) is used to improve accuracy of radical radiotherapy by adjusting treatment to the observed imaging changes. To ensure appropriate adjustment, image interpretation should precede any changes to treatment delivery. This study provides the methodology for image interpretation and the frequency and evolution of the changes in patients undergoing radical radiotherapy for localised and locally advanced non-small cell lung cancer (NSCLC).

*Patients and methods*

From December 2012 to December 2014, 250 patients with localised and locally advanced NSCLC had 2462 chest CBCT scans during the course of fractionated radical radiotherapy (RT) (3 – 5 daily CBCTs in the first week followed by at least weekly imaging, mean 9.5 per patient, range 1-21). All CBCT images were reviewed describing changes and their evolution using diagnostic imaging definitions and validated by an independent chest radiologist.

*Results*

During radical RT for NSCLC 328 imaging changes were identified on CBCT in 180 (72%) patients; 104 (32%) had reduction and 41 (13%) increase in tumour size; 48 (15%) had changes in consolidations contiguous to the primary lesion, 26 (8%) non-contiguous consolidations, 43 (13%) changes in tumour cavitation, 36 (11%) pleural effusion and 30 (9%) changes in atelectasis.

In 105 patients imaging changes were noted in continuity with the treated tumour of which only 41 (39%) represented tumour enlargement; others included new or enlarging adjacent consolidation (34%), and new or enlarging atelectasis (19%). The changes evolved during treatment.

*Conclusion*

Imaging changes on CBCT include real and apparent changes in tumour size and parenchymal changes which evolve during treatment. Correct image interpretation, particularly when occurring adjacent to the tumour, is essential prior to adjustment to treatment delivery.

## Introduction

High dose fractionated external beam radiotherapy with or without chemotherapy remains the mainstay of radical treatment of localised and locally advanced non-small cell lung cancer (NSCLC) not amenable to surgical excision [1].

Successful outcome demands accurate tumour localisation and precise delivery of treatment. These are dependent on the quality of imaging determined both by technical and operator related factors. In the treatment of lung cancer the imaging modality of choice to define the target and critical normal structures currently remains CT scanning. While the technical aspects of CT imaging continue to improve to allow better visualisation of thoracic structures, operator dependent image interpretation has been subject to less academic scrutiny, yet this is likely to be an important determinant of accuracy of radiotherapy delivery.

The principal focus of the accuracy and reliability of image interpretation which defines the target for treatment has been on pre-treatment imaging where target outlining is an integral component of the treatment planning process. An increasingly important aspect of radiotherapy imaging which guides the quality of radiotherapy delivery is image guidance during treatment currently using cone beam CT (CBCT) mounted on the linear accelerator [2]. As with pre-treatment CT, the accuracy of treatment relies on adjusting radiotherapy delivery to information obtained from the CBCT image and this demands not only high quality imaging but also correct and reliable image interpretation. This expertise rests either with the radiation oncologist or in many centres with the radiation therapist/technologist.

CBCT image interpretation has been entirely in the hands of the treating profession and not subject to assessment and validation by imaging experts (radiologists). It is therefore a largely non-validated skill which is open to significant interobserver variation and potential incorrect interpretation of the images. To ensure the image interpretation complies with validated imaging criteria the study was designed and conducted together with an expert thoracic radiologist.

The study examined in detail over 2000 CBCT images in 250 patients undergoing radical radiotherapy for locally advanced NSCLC describing imaging changes and their evolution using validated imaging definitions and assessed and quality assured by an expert thoracic radiologist. This should provide the basis for accurate and reliable interpretation of CBCT images during treatment to ensure appropriate adjustment of treatment to enable optimum treatment outcome both in terms of best tumour control and minimal treatment related toxicity.

**Patients and methods**

*Study population*

**Table 1**

Patient & disease characteristics of a cohort of 250 patients with NSCLC treated with radical radiotherapy

| *Characteristic* | Number of pts. | % |
|---|---|---|
| **Gender** | **250** | 100% |
| F | 115 | 46% |
| M | 135 | 54% |
| **WHO performance status (PS)** | | |
| 0 | 58 | 23% |
| 1 | 90 | 36% |
| 2 | 81 | 32% |
| 3 | 9 | 4% |
| NA | 12 | 5% |
| **COPD comorbidity** | | |
| yes | 65 | 26% |
| no | 185 | 74% |
| **Histology** | | |
| adenocarcinoma | 86 | 34% |
| squamous cell carcinoma | 119 | 48% |
| NSCLC NOS | 24 | 10% |
| large cell carcinoma | 2 | 1% |
| adenosquamous carcinoma | 3 | 1% |
| carcinosarcoma | 1 | 0% |
| not histologically verified | 15 | 6% |
| **AJCC stage** | | |
| IA | 10 | 4% |
| IB | 25 | 10% |
| IIA | 14 | 6% |
| IIB | 24 | 10% |
| IIIA | 120 | 48% |
| IIIB | 47 | 19% |
| IV | 10 | 4% |
| **Chemotherapy** | | |
| concurrent chemoradiotherapy | 51 | 20% |
| sequential chemoradiotherapy | 107 | 43% |
| TKI | 1 | 0% |
| **RT dose fractionation** | | |
| 50 – 55 in 20 fractions | 242 | 97% |
| 58 – 60Gy in 20 – 30 fractions | 8 | 3% |

The study was a structured review of all available diagnostic, planning, cone beam and post-treatment CT scans in a cohort of patients undergoing conventional fractionated radical external beam radiotherapy (Table 1) for histologically verified NSCLC (with or without neoadjuvant & concomitant chemotherapy – Table 1) between 31/12/2012 and 30/12/2014 with CBCTs obtained in the two calendar years. All patients had an identifiable tumour on CT imaging. Patients undergoing SABR and palliative radiotherapy were excluded from the analysis as were patients without an identifiable lung parenchymal tumour (adjuvant radiotherapy for microscopic residual disease after surgery), and those who received previous thoracic or adjacent radiotherapy (e.g. for breast cancer).

*Imaging*

All patients had planning CT scan with Philips Brilliance CT scanner (Philips N.V., Eindhoven, NL). On treatment cone beam CT scans were performed using Varian Truebeam and Varian C-series Linac with kV X-ray source OBI (Varian Medical Systems, Palo Alto, California, USA). The general policy was to perform 3 – 5 daily CBCTs in the first week followed by at least weekly imaging (more when changes were detected requiring potential treatment adjustment) with a mean of 9.5 per patient (range 1-21). Following radiotherapy diagnostic CT was carried out 1 – 6 months after completion of treatment with a median of 73 days (patients usually have imaging 3 months after treatment but some had it earlier due to symptoms or had it at their local hospital first).

All images were scored and reviewed by one IGRT experienced specialist clinical oncologist (EC) with contentious cases reviewed by a thoracic radiologist (JC) or another clinical oncologist (MB). The imaging from a randomly selected 10% of the patients was reviewed by an expert thoracic radiologist (JC).

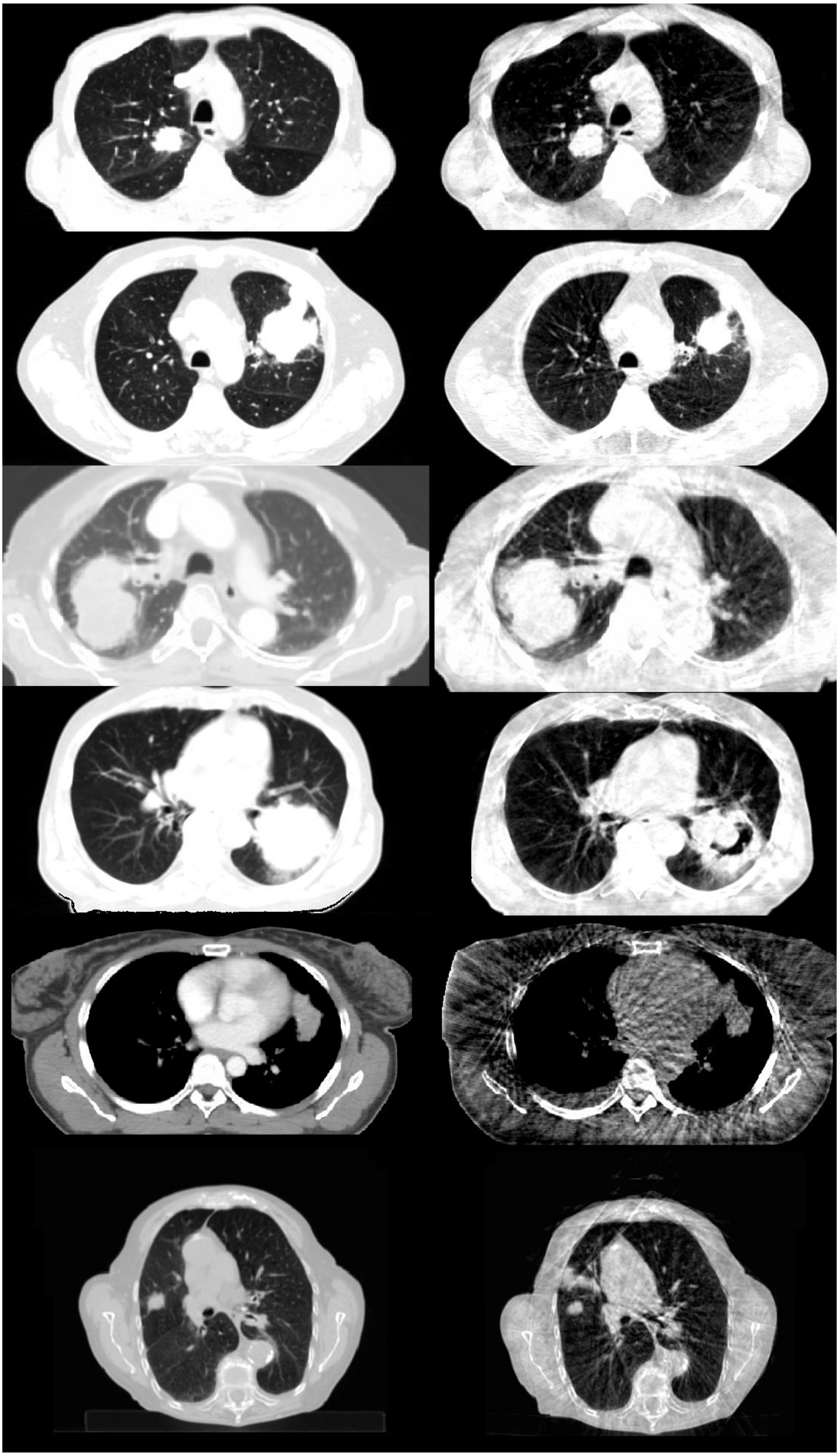
*Imaging abnormalities*

Imaging abnormalities on planning CT and on CBCT during RT were identified and recorded using standard imaging terminology [3]. Changes were reported in comparison to planning CT and the previous CBCT. Due to the limited resolution of CBCT images only changes ≥ 3 mm were considered significant. Examples are shown in Figure 1.

**Figure 1**

Examples of imaging changes during radical radiotherapy for NSCLC. Planning CT images are shown on the left and cone beam CT scan images on the right.

A tumour enlargement; B reduction in tumour size; C new contiguous consolidation; D cavitation; E contralateral pleural effusion; F atelectasis.



Tumour enlargement (or progression) was defined as concentric (involving more than 50% of the margin) increase of ≥ 3 mm of either maximum diameter or perpendicular maximum diameter of the primary tumour. Similarly tumour reduction (or regression) was defined as a decrease in size ≥ 3 mm of maximum or perpendicular maximum diameter of the primary tumour.

Consolidation (or infiltrative change) was classified as contiguous and non-contiguous. Contiguous consolidation was defined as increase in pulmonary parenchymal attenuation, generally homogeneous, that obscures the margins of vessels and airway walls of at least 3 mm, not considered to be tumour or atelectasis, contiguous with the tumour, or a nonconcentric increase in size of the tumour at least 3 mm affecting less than 50% of the tumour margin.

Non-contiguous consolidation was defined as increased parenchymal attenuation of at least 3 mm not considered to be tumour or atelectasis contiguous with the tumour.

Cavitation was defined as a gas-filled space seen as a lucency or low-attenuation area within the tumour of at least 3mm.

Pleural effusion was defined as the presence of at least 3mm of fluid-like density between lung and posterior chest wall (on a supine CT scan).

Atelectasis had the characteristics of consolidation with distinguishing anatomical features often associated with abnormal displacement of fissures, bronchi, vessels, diaphragm, heart, or mediastinum.

*Quality assurance*

Series of planning, cone beam and post treatment scans from 10% of randomly selected patients (25) were reviewed by an experienced thoracic radiologist (JC). Complete concordance was noted in 10 patients. In the remaining 15 patients, 23 out of 30 changes were agreed and 7 were amended (4 were added). The overall error rate was < 10% and mostly related to lung changes not adjacent to the tumour. Following the review of cases the whole image dataset was reviewed with minor amendment and this data is presented.

*Statistical analysis*

SPSS version 21.0, (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. $\chi 2$ test and Spearman's rank correlation coefficients were used to assess correlations between imaging changes and patient, tumour and treatment characteristics .

## Results

*Patients*

Over a 2 year period (31/12/2012 to 30/12/2014) 430 patients with NSCLC had chest CBCT scans during the course of RT. Two hundred and fifty met the inclusion criteria. The patient and disease characteristics are shown in Table 1. The majority (67%) had stage III disease; 51 (20%) received concurrent chemo-radiotherapy and 107 (43%) sequential chemoradiation. The majority of patients (241 - 96%) received a dose of 50-55Gy in 20 fractions.

Most patients completed the full course of treatment. The treatment was discontinued early in 8 patients due to treatment related toxicity (2), disease progression (2), increased dyspnoea (1) and other reasons (3).

The majority of patients (170) had a 3D planning scan; 80 had a 4D planning CT scan. Overall 2378 3D CBCT scans were reviewed (mean 9.5 per patient); 50 patients had 4DCBCT for a total number of 84 scans (1-3 per patient). If two CBCT (due to beam repositioning) were performed on the same day only the original image was analysed and reported.

*Planning CT scan*

On the planning CT scan 363 abnormalities were noted in 212 patients. Contiguous consolidation was noted in 125 and non-contiguous in 118 patients; 40 patients had tumour cavitation, 32 effusion and 48 atelectasis; 106 patients had one, 67 two, 33 three and 6 four abnormalities. 38 patients had no abnormalities on planning CT (Appendix, Table I).

*On treatment cone beam CT (CBCT) scan*

Out of 250 patients 180 (72%) had at least one change on CBCT during radiotherapy compared to the planning CT scan. This included both new abnormalities and a change in size of an existing abnormality (≥ 3mm). Overall 328 changes were identified: 145 were alterations in the size of the primary lesion (104 reductions and 41 enlargements) and 183 were changes not directly involving the tumour mass. Of these 60 were new (not seen on planning CT) and 123 were changes of previously identified abnormalities.

Contiguous consolidation was seen in 48 patients (14 new, 30 increases and 4 reductions of pre-existing contiguous consolidation) and non-contiguous consolidations in 26 (5 new, 19 increases and 2 reductions of pre-existing). Cavitation was noted in 43 patients (14 new, 9 increases, 20 reductions or disappearance/resolution of pre-existing cavities), pleural effusion in 36 (21 new, 10 increases, 5 reductions) and atelectasis in 30 patients (6 new, 14 increases and 10 reductions). Seventy patients had no changes during RT, 79 had one change, 66 had two, 24 three, 10 four and 1 patient had five changes (Table 2).

**Table 2**

Imaging changes on CBCT (250 patients; 328 changes) during radical radiotherapy for NSCLC

| change in tumour size | Number of changes | % changes | % patients |
|---|---|---|---|
| enlargement | 41 | 13% | |
| reduction | 104 | 32% | |
| **Total** | 145 | 44% | 58% |
| **contiguous consolidation** | | | |
| new | 14 | 4% | |
| pre-existing increased | 30 | 9% | |
| pre-existing decreased | 4 | 1% | |
| **Total** | 48 | 15% | 19% |
| **non-contiguous consolidation** | | | |
| new | 5 | 2% | |
| pre-existing increased | 19 | 6% | |
| pre-existing decreased | 2 | 1% | |
| **Total** | 26 | 8% | 10% |
| **cavitation** | | | |
| new | 14 | 4% | |
| pre-existing increased | 9 | 3% | |
| pre-existing decreased | 20 | 6% | |
| **Total** | 43 | 13% | 17% |
| **pleural effusion** | | | |
| new | 21 | 6% | |
| pre-existing increased | 10 | 3% | |
| pre-existing decreased | 5 | 2% | |
| **Total** | 36 | 11% | 14% |
| **atelectasis** | | | |
| new | 6 | 2% | |
| pre-existing increased | 14 | 4% | |
| pre-existing decreased | 10 | 3% | |
| **Total** | 30 | 9% | 12% |

*Lung parenchymal changes*

Of 125 patients without contiguous consolidation on the planning CT scan 14 (11%) developed contiguous consolidation during RT. Of 125 patients with a pre-existing contiguous consolidation 30 (24%) had an increase and 4 (3%) a reduction. In total 44 of 250 patients (18%) had a new or an increase in size of a contiguous consolidation during RT. Overall, 48 (19%) patients had changes in the lung parenchyma adjacent to the tumour not representing an alteration in tumour size.

Of 132 patients without a non-contiguous consolidation on the planning CT scan 5 (4%) developed a non-contiguous consolidation during RT. In 19 (16%) of 118 patients with a pre-existing non-contiguous consolidation there was an increase (11 in number of lesions and 8 in size of lesions) and in 2 a reduction in size during radiotherapy. In total 40 patients (16%) developed a new non-contiguous consolidation.

Of 202 patients without pre-existing atelectasis on the planning CT scan 6 (3%) developed a new atelectasis during treatment. In 48 patients with a pre-existent atelectasis, 14 (29%) had an increase and 10 (21%) a decrease in atelectasis size. In total 20 patients (8%) developed a new atelectasis or increase in size of a pre-existing atelectasis during treatment.

The median time interval between planning-CT and start of the treatment (first CBCT) was 14 days (range 5–27 days). A significant correlation was found between longer time interval and development of changes ($p = 0.011$). There was no significant correlation found with patient characteristics, but there was a trend with advanced T stage and changes ($p= 0.06$).

*Changes within or adjacent to the treated tumour*

In 105 patients imaging changes were noted within or adjacent to the treated tumour; in 41 (39%) patients these represented tumour enlargement while in 14 (13%) patients the changes were new and in 30 (29%) enlarging adjacent consolidation and in 20 (19%) new or enlarging atelectasis (Table 2).

*Timing and evolution of changes*

Enlargement of the primary lesion was noted almost exclusively at the first fraction (40 patients out of 41). Most reductions were noted in the second half of treatment with a median time of onset in the third week of treatment. Of 41 patients with tumour enlargement the lesion became smaller during treatment in 31, remained stable in 8 and progressed in 2. Of the total of 250 patients reduction in the size by the last week of treatment was noted in 126 (50%) patients.

Changes adjacent to the tumour mass in the form of contiguous consolidation were noted at the first fraction in 29 (60%) patients and during the first week in 33 (69%), with further 6 in the second, 7 in the third and 2 on the fourth week of treatment. Of 44 patients with new or changed contiguous consolidation (enlarged pre-existing and new) in 20 patients this decreased in size over the course of treatment.

The evolution of changes in non-contiguous consolidation and in atelectasis followed a similar pattern. Of 20 patients with enlarging and new atelectasis this fully or partially resolved in 9 patients over the course of treatment.

**Discussion**

CBCT is used primarily for adjustment of radiotherapy delivery to ensure accurate targeting of the tumour and optimal normal tissue avoidance [2]. Identification and interpretation of the changes observed on CBCT is essential prior to altering treatment to ensure the adjustments made are appropriate. We report a systematic description and analysis of imaging abnormalities seen on CBCT and their evolution during and after radical RT in patients with locally advanced NSCLC. The CBCT images were treated as "diagnostic" scans using validated imaging descriptors in consultation with a thoracic radiologist. The aim was to improve the understanding of CBCT images and thereby improve the practice of image guided radiotherapy (IGRT) which may result in better treatment outcomes. The study did not focus on shifts and treatment adjustment although the interpretation of imaging changes has a direct implication for treatment delivery.

Radiological changes on CBCT are common (observed in 72% of patients). Less than half (44%) represent changes in tumour size which may lead to adjustment to treatment delivery. Just over half of the changes (56%) did not represent a change in tumour size. Of these two thirds were changes in abnormalities identified on planning CT and a third were abnormalities first noted during treatment. Intra-thoracic anatomical changes were reported on CBCT in 72% of patients treated with radiotherapy [4] with the purpose of defining changes that may need action ("Traffic Light Protocol"). These focussed principally on changes in tumour size and atelectasis though did not distinguish parenchymal changes adjacent to the tumour (contiguous consolidation) which may mimic alteration in tumour size and did not formally involve diagnostic imaging criteria.

Identification of potential tumour enlargement during treatment is of particular relevance to IGRT in NSCLC [4-6]. Missing a true enlargement not encompassed within the PTV may result in undertreatment while treatment adjustment to encompass apparent enlargement due to contiguous consolidation or atelectasis may lead to unnecessary treatment of normal tissues with a potential risk of increased toxicity. In the cohort studied increase in the size of the tumour and the adjacent opacities was noted in 85 patient and of these 41 represented increase in tumour size and 44 new or enlarged contiguous consolidation (Table 2). It can be concluded that more than half of the changes which suggest an apparent increase in tumour size are not due to tumour enlargement and therefore do not require adjustment to the target volume.

Identification and correct interpretation of the evolution of imaging changes on CBCT during radiotherapy is of equal importance to the delivery of radiotherapy as parenchymal changes such as change in consolidation require different action than changes in tumour size.

Increase in tumour size noted principally at the beginning of treatment is likely to reflect tumour growth in the period prior to commencing radiotherapy. Tumours tend to decrease in size mostly towards the end of the treatment [4,5,7-14]. Lung parenchymal changes also occur more frequently in the early stages of treatment and mostly tend to improve or resolve during the course of treatment (Appendix, Table III) [4,5,15,16]. Our analysis of diagnostic imaging after treatment (Appendix, Table IVb) noted a continuing trend in reduction in the size of the tumour though a proportion remain stable.

The complexity of evolution of lung parenchymal changes before (Appendix, Table I) and after RT (Appendix, Table IVa) suggests that the evolution of changes is affected by a number of factors related to disease, treatment and comorbidity (such as COPD).

The current study does not provide information on the clinical significance of lung parenchymal changes - contiguous and non-contiguous consolidation (68) and new or enlarging atelectasis (20) (Table 2). The majority of patients did not receive additional therapy such as antibiotics although this data was not comprehensively recorded. On the basis of the available information treatment with antibiotics for potential infective cause and the use of anticoagulants for thromboembolic disease should be principally guided by symptoms in the context of comorbidity (e.g. COPD) and appropriate diagnostic imaging rather than CBCT imaging abnormalities alone. The management of imaging changes requires a separate prospective study. The issue of adaptive radiotherapy for reduction in tumour size (seen in 104 (42%) of patients (Table 2)) is currently open to debate and awaits results of prospective trials.

CBCT images are subject to artefact and while the image quality continues to improve it does not yet reach the quality of diagnostic CT [17]. In terms of the results reported here the presence of artefacts (not scored) may have resulted in some misreporting although the collaboration with and review by an experienced thoracic radiologist minimised such potential errors.

We conclude that fast image analysis and interpretation of on-line or off-line CBCT is challenging and this may be compounded by the quality of CBCT images. The likelihood of misreporting in the clinical situation is therefore considerable and potentially greater than reported here. The data presented highlights the need for correct image interpretation which can be achieved by more detailed image inspection and analysis combined with appropriate training of personnel involved in lung IGRT. The aim to improve accuracy of treatment delivery by adjustment based on CBCT should be a two step process. The first and critical step prior to adjustment requires "diagnostic" type image interpretation and this study provides information on the frequency of the observed changes only some of which require adjustment to treatment delivery.

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**APPENDIX**

**Table I**

Abnormalities on planning CT scan and number of abnormalities per patient as absolute numbers and percentage in relation to total number of patients (250) and abnormalities (363).

| **abnormalities on planning CT** | **n abnormalities** | **% patients** | **% abnormalities** |
|---|---|---|---|
| contiguous consolidation | 125 | 50% | 34% |
| non-contiguous consolidation | 118 | 47% | 33% |
| cavitation | 40 | 16% | 11% |
| effusion | 32 | 13% | 9% |
| atelectasis | 48 | 19% | 13% |
| Total changes | 363 | | 100% |

| **n abnormalities on planning CT** | **n pts** | **% patients** |
|---|---|---|
| 0 | 38 | 15% |
| 1 | 106 | 42% |
| 2 | 67 | 27% |
| 3 | 33 | 13% |
| 4 | 6 | 2% |
| **Total** | **250** | **100%** |
| any abnormality (1-4) | 212 | 85% |

**Table II**

Timing of changes during treatment as absolute numbers and percentage in relation to total number of changes (328), described by number of week of onset, onset on first fraction and median fraction. (cont cons: contiguous consolidation; dist cons: distant consolidation; pleural eff: pleural effusion)

| | *1st #* | | 1st week | | 2nd week | | 3rd week | | 4th week | | total | median |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Change | *n* | *%* | n | % | n | % | n | % | n | % | n | n fraction |
| enlargement | *40* | *98%* | 40 | 98% | 1 | 2% | 0 | 0% | 0 | 0% | 41 | 1 |
| reduction | *2* | *2%* | 7 | 7% | 24 | 23% | 42 | 40% | 31 | 30% | 104 | 14 |
| cont cons | *29* | *60%* | 33 | 69% | 6 | 13% | 7 | 15% | 2 | 4% | 48 | 1 |
| dist cons | *10* | *38%* | 15 | 58% | 5 | 19% | 2 | 8% | 4 | 15% | 26 | 4 |
| cavitation | *24* | *56%* | 27 | 63% | 3 | 7% | 4 | 9% | 9 | 21% | 43 | 1 |
| pleural eff | *13* | *36%* | 26 | 72% | 6 | 17% | 1 | 3% | 3 | 8% | 36 | 3 |
| atelect | *19* | *63%* | 20 | 67% | 3 | 10% | 4 | 13% | 3 | 10% | 30 | 1 |
| TOT | *137* | *42%* | 168 | 51% | 48 | 15% | 60 | 18% | 52 | 16% | 328 | 5 |

**Table III**

Evolution of changes on cone beam CT during treatment (comparing CBCT with CBCT) as absolute numbers and percentage in relation to number of changes of the same group.

| **Lesion enlargement** | n | % |
|---|---|---|
| stable | 8 | 20% |
| increasing | 1 | 2% |
| reduction, then increase again | 1 | 2% |
| reduction to initial size | 9 | 22% |
| further reduction | 22 | 54% |
| **Total** | 41 | 100% |

| **Lesion reduction** | n | % |
|---|---|---|
| Stable or further reduction | 104 | 100% |

| **new contiguous consolidation** | n | % |
|---|---|---|
| persistent consolidation during RT (stable) | 5 | 36% |
| disappearance of consolidation | 9 | 64% |
| **Total** | 14 | 100% |

| **increased contiguous consolidation** | n | % |
|---|---|---|
| persistent increase during RT (stable) | 19 | 63% |
| reduction to initial size (as planning CT) | 6 | 20% |
| reduction to smaller size than planning CT | 5 | 17% |
| **Total** | 30 | 100% |

| **decreased contiguous consolidation** | n | % |
|---|---|---|
| stable | 4 | 100% |

| **new non-contiguous consolidation** | n | % |
|---|---|---|
| stable | 5 | 100% |

| **Increase in number of non-contiguous consolidation** | n | % |
|---|---|---|
| stable | 8 | 73% |
| slight reduction (still more compared to planning CT) | 1 | 9% |
| reduction as initial | 2 | 18% |
| **Total** | 11 | 100% |

| **Increase in size of non-contiguous consolidation** | n | % |
|---|---|---|
| stable | 4 | 50% |
| reduction as initial | 4 | 50% |
| **Total** | 8 | 100% |

| **Decrease in size of non-contiguous consolidation** | n | % |
|---|---|---|
| stable | 1 | 50% |
| increase | 1 | 50% |
| **Total** | 2 | 100% |

| **new cavitation** | n | % |
|---|---|---|
| stable | 11 | 79% |
| disappearance | 3 | 21% |
| **Total** | 14 | 100% |

| **increased cavitation** | n | % |
|---|---|---|
| stable | 5 | 56% |
| reduction as initial | 2 | 22% |
| further reduction | 2 | 22% |
| **Total** | 9 | 100% |

| **decresead cavitation** | n | % |
|---|---|---|
| stable | 5 | 36% |
| disappearance | 6 | 43% |
| increase to initial size | 1 | 7% |
| further increase | 2 | 14% |
| **Total** | 14 | 100% |

| **Disappearance of cavitation** | n | % |
|---|---|---|
| stable | 2 | 33% |
| reappearance but less than initial | 1 | 17% |
| reapparance bigger than initial | 3 | 50% |
| **Total** | 6 | 100% |

| **new pleural effusion** | n | % |
|---|---|---|
| stable | 14 | 67% |
| disappearance | 6 | 29% |
| reduction but still present | 1 | 5% |
| **Total** | 21 | 100% |

| **increased pleural effusion** | n | % |
|---|---|---|
| stable | 8 | 80% |
| reduction to initial size | 2 | 20% |
| **Total** | 10 | 100% |

| **decreased pleural effusion** | n | % |
|---|---|---|
| stable | 2 | 67% |
| more-less effusion | 1 | 33% |
| **Total** | 3 | 100% |

| **disappearance of effusion** | n | % |
|---|---|---|
| stable | 2 | 100% |

| **new atelectasis** | n | % |
|---|---|---|
| stable | 4 | 67% |
| disappearance | 2 | 33% |
| **Total** | 6 | 100% |

| **increased atelectasis** | n | % |
|---|---|---|
| stable | 6 | 43% |
| reduction to initial size | 3 | 21% |
| further reduction | 4 | 29% |
| reduction then increase | 1 | 7% |
| **Total** | 14 | 100% |

| **decreased atelectasis** | n | % |
|---|---|---|
| stable | 10 | 100% |

**Table IVa**

**Evolution of changes after treatment** (diagnostic CT scans after RT compared with CBCT during RT and planning CT scan) as absolute numbers and percentage in relation to number of changes of the same group.

| **lesion enlargement** | n | % |
|---|---|---|
| progression | 4 | 10% |
| reduction | 33 | 80% |
| stable | 2 | 5% |
| no data | 2 | 5% |
| **Total** | 41 | 100% |

| **lesion reduction** | n | % |
|---|---|---|
| progression | 4 | 4% |
| further reduction | 83 | 80% |
| stable reduction | 7 | 7% |
| stable lesion | 1 | 1% |
| NA (consolidation) | 3 | 3% |
| no data | 6 | 6% |
| **Total** | 104 | 100% |

| **new contiguous consolidation** | n | % |
|---|---|---|
| increase in size of consolidation | 5 | 36% |
| stable consolidation | 3 | 21% |
| decrease in size of consolidation | 2 | 14% |
| disappearance of consolidation | 4 | 29% |
| **Total** | 14 | 100% |

| **increased contiguous consolidation** | n | % |
|---|---|---|
| further increase (>CBCT, >CT) | 16 | 53% |
| stable increase (=CBCT, >CT) | 3 | 10% |
| slight reduction (<CBCT, >CT) | 2 | 7% |
| reduction to initial (<CBCT, =CT) | 3 | 10% |
| further reduction (<CBCT, <CT) | 3 | 10% |
| disappearance of consolidation | 1 | 3% |
| no data | 2 | 7% |
| **Total** | 30 | 100% |

| **decreased contiguous consolidation** | n | % |
|---|---|---|
| further reduction (<CBCT, <CT) | 1 | 25% |
| slight increase (>CBCT, <CT) | 1 | 25% |
| further increase (>CBCT, >CT) | 2 | 50% |
| **Total** | 4 | 100% |

| **new non-contiguous consolidation** | n | % |
|---|---|---|

| | | |
|---|---|---|
| stable consolidation | 1 | 20% |
| decrease in size of consolidation | 1 | 20% |
| decrease in number of consolidation | 1 | 20% |
| disappearance of consolidation | 2 | 40% |
| **Total** | 5 | 100% |

| **increased non-contiguous consolidation** | n | % |
|---|---|---|
| further increase (>CBCT, >CT) | 5 | 26% |
| stable increase (=CBCT, >CT) | 7 | 37% |
| slight reduction (<CBCT, >CT) | 1 | 5% |
| reduction to initial (<CBCT, =CT) | 3 | 16% |
| disappearance of all consolidations | 2 | 11% |
| no data | 1 | 5% |
| **Total** | 19 | 100% |

| **decreased non-contiguous consolidation** | n | % |
|---|---|---|
| further reduction (<CBCT, <CT) | 1 | 50% |
| increase (>CBCT, >CT) | 1 | 50% |
| **Total** | 2 | 100% |

| **new cavitation** | n | % |
|---|---|---|
| increase in size of cavitation | 3 | 21% |
| stable cavitation | 1 | 7% |
| decrease in size of cavitation | 4 | 29% |
| disappearance of cavitation | 6 | 43% |
| **Total** | 14 | 100% |

| **increased cavitation** | n | % |
|---|---|---|
| further increase (>CBCT, >CT) | 2 | 22% |
| stable increase (=CBCT, >CT) | 1 | 11% |
| reduction to initial (<CBCT, =CT) | 1 | 11% |
| further reduction (<CBCT, <CT) | 2 | 22% |
| disappearance of cavitation | 2 | 22% |
| no data | 1 | 11% |
| **Total** | 9 | 100% |

| **decreased cavitation** | n | % |
|---|---|---|
| disappearance of cavitation | 7 | 50% |
| stable reduction (=CBCT, <CT) | 4 | 29% |
| increase (>CBCT, >CT) | 2 | 14% |
| no data | 1 | 7% |
| **Total** | 14 | 100% |

| **disappearance of cavitation** | n | % |
|---|---|---|
| stable (no cavity) | 2 | 33% |
| reapparance (<CT) | 2 | 33% |
| further increase (>CT) | 1 | 17% |
| no data | 1 | 17% |
| **Total** | 6 | 100% |

| **new pleural effusion** | n | % |
|---|---|---|
| increase in size of effusion | 3 | 14% |
| stable effusion | 5 | 24% |
| decrease in size of effusion | 3 | 14% |
| disappearance of effusion | 10 | 48% |
| **Total** | 21 | 100% |

| **increased pleural effusion** | n | % |
|---|---|---|
| further increase (>CBCT, >CT) | 2 | 20% |
| slight reduction (<CBCT, >CT) | 3 | 30% |
| reduction to initial (<CBCT, =CT) | 2 | 20% |
| further reduction (<CBCT, <CT) | 2 | 20% |
| disappearance of effusion | 1 | 10% |
| **Total** | 10 | 100% |

| **decreased pleural effusion** | n | % |
|---|---|---|
| further reduction (<CBCT, <CT) | 2 | 67% |
| disappearance of pleural effusion | 1 | 33% |
| **Total** | 3 | 100% |

| **disappearance of effusion** | n | % |
|---|---|---|
| stable (no effusion) | 2 | 100% |
| **Total** | 2 | 100% |

| **new atelectasis** | n | % |
|---|---|---|
| increase in size of atelectasis | 1 | 17% |
| stable atelectasis | 1 | 17% |
| decrease in size of atelectasis | 1 | 17% |
| disappearance of atelectasis | 2 | 33% |
| no data | 1 | 17% |
| **Total** | 6 | 100% |

| **increased atelectasis** | n | % |
|---|---|---|
| further increase (>CBCT, >CT) | 3 | 21% |
| stable increase (=CBCT, >CT) | 2 | 14% |
| slight reduction (<CBCT, >CT) | 1 | 7% |
| reduction to initial (<CBCT, =CT) | 2 | 14% |

| | | |
|---|---|---|
| further reduction (<CBCT, <CT) | 5 | 36% |
| disappearance of atelectasis | 1 | 7% |
| **Total** | 14 | 100% |

| **decreased atelectasis** | n | % |
|---|---|---|
| further reduction | 5 | 50% |
| disappearance of atelectasis | 1 | 10% |
| stable reduction (=CBCT, <CT) | 3 | 30% |
| increase (>CBCT, >CT) | 1 | 10% |
| **Total** | 10 | 100% |

**Table IVb**

**Evolution of tumour after treatment (comparing diagnostic CT scans after RT with CBCT during RT and planning CT scan) in patients who had no change in size of the tumour during RT (105) and in patients who had no radiological changes during RT (70),** as absolute numbers and percentage in relation to number of patients of the same group.

| **no. change in size during RT** | n | % |
|---|---|---|
| progression | 2 | 2% |
| reduction | 49 | 47% |
| stable lesion | 33 | 31% |
| NA (consolidation) | 10 | 10% |
| no data | 11 | 10% |
| **TOT** | 105 | 100% |

| **no change** | n | % |
|---|---|---|
| progression | 0 | 0% |
| reduction | 36 | 51% |
| stable lesion | 17 | 24% |
| NA (consolidation) | 6 | 9% |
| no data | 11 | 16% |
| **TOT** | 70 | 100% |