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## Accuracy in suspicious lung infiltrations

We read with interest the paper by Targowski *et al*.<sup>1</sup> Suspicious lung infiltrations such as malignant tumours are always difficult to diagnose in clinical practice. Transthoracic fine needle biopsy (TFNB) may be a useful procedure despite a high risk of false negative results. To improve the accuracy of the technique, telomerase activity in combination with TFNB was investigated in the study by Targowski *et al*.

We suggest that alternative options such as positron tomography scanning (CT-PET) should be evaluated, which may provide better imaging quality and accurate guidance for performing TFNB, increasing the accuracy of lung cancer diagnosis.

In the Continuing Observation of Smoking Subjects (COSMOS) study recently published by Veronesi *et al*<sup>2</sup> involving 5200 current or former smokers, CT-PET had a sensitivity of 100% in the diagnosis of solid pulmonary nodules of 10 mm or more. In this study, TFNB was not part of the clinical routine. In contrast, the sensitivity of the combination of TFNB with telomerase activity used by Targowski *et al* was lower at 89.3% and the mean size of suspected lesions was not described.

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## Authors' reply

We read with interest the comment by Dr Carbone *et al* on our article<sup>1</sup> and agree that nowadays CT-PET is the best imaging method for visualisation of suspected pulmonary nodules.

Transthoracic fine needle aspiration (TFNB) under CT-PET control could improve the accuracy of lung cancer diagnosis, especially in cases of solid lesions with a smaller standardised uptake value (SUV). Some data suggest that even 50% of pulmonary nodules with SUV <2.5 are benign.<sup>2</sup>

In the Continuing Observation of Smoking Subjects (COSMOS) study by Veronesi *et al*,<sup>3</sup> CT-PET had a sensitivity of 100% in the diagnosis of solid pulmonary nodules of 10 mm or more. In our study the mean size of suspected lesions (described at the beginning of the Results section) was 2.4 cm (95% CI 2.2 to 2.5), which was comparable to data in the study by Veronesi *et al* (2.5 cm, range 0.6–6 cm), but the indication for TFNB was not only restricted to solid nodules. The sensitivity, specificity and accuracy of cytological and telomerase activity examinations in our study was adequate (89.3%, 96.9%, 90%, respectively) and was similar to the overall results achieved by Veronesi *et al* (88%, 93% and 91%, respectively). The diagnostic value of telomerase activity assessments in pulmonary tumours is only one of many benefits. Data show that telomerase activity in material derived from pulmonary nodules is also a prognostic factor for survival<sup>4</sup> and could be a target for antitelomerase treatment.<sup>5</sup>

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## Dysfunctional breathing in patients with asthma

We recognise and applaud the efforts of Holloway and West<sup>1</sup> and are encouraged by their findings. We agree that further investigation is warranted but that greater scientific methodology needs to be applied. Hyperventilation appears to be the only form of dysfunctional breathing that most physicians recognise yet even within this label, acute and chronic hyperventilation are physiologically distinct.<sup>2</sup> Efforts must be made to further elucidate the nature of dysfunctional breathing in its many forms<sup>3</sup>

and direct appropriate therapy towards appropriate patients. It is a reasonable assumption that breathing retraining will be efficacious only in those patients where dysfunctional breathing exists. This lends support to the positive results of Holloway and West,<sup>1</sup> given the unselected nature of the cohort of subjects recruited. It is hardly surprising that many trials of breathing retraining in unselected asthmatics prove equivocal. We liken this approach to a trial of thrombolytic therapy in unselected chest pain patients.

As a sub-note, we would guard against making assumptions on the basis of a reduction in Nijmegen scores. The Nijmegen questionnaire has only ever been validated in primary hyperventilation and even then the gold standard was physician interpreted typical symptoms.<sup>4</sup> It was only described as a threshold value for the diagnosis of hyperventilation and there is no evidence that there is a graded correlation between Nijmegen scores and symptom severity. The domains within the questionnaire overlap with asthma symptoms. We have found it not to be predictive of capnography in patients with severe asthma. Since there is a trend towards improved spirometric values in the study group of Holloway and West,<sup>1</sup> we would suggest caution in interpreting a reduction in Nijmegen scores as a positive signal of reduced dysfunctional breathing.

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## Use of long-acting $\beta_2$ agonists in arginine-16 homozygous patients with asthma

We read with interest the study by Palmer and colleagues.<sup>1</sup> Their findings suggest that patients who are Arg/Arg homozygous at position 16 of the  $\beta_2$  adrenoceptor may be at increased risk of asthma exacerbations,