Reviewer’s report

Title: Lung diffusing capacity for nitric oxide and carbon monoxide in relation to morphological changes as assessed by computed tomography in patients with cystic fibrosis

Version: 2 Date: 14 August 2008

Reviewer: Harm AWM Tiddens

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The authors aim to study the relationship between Dlno, DLco vs CT

General comments
The rational to identify a new diffusion marker for CF lung disease is interesting. The major aim of the lung is diffusion and thus it makes sense to monitor this capacity.

This is a cross sectional study in an adult population of CF patients. Inclusion criteria were when a CT was available not older than 3 years. Hence, there was a substantial time interval between CT and PFT.

Major comments
What were the indications of the CT. Is it done routinely? Or were some of the CTs taken during exacerbations. This needs to be specified.

A major weakness of the study is its retrospective nature. Up to three years time interval is allowed between CT and PFTs. In addition it is not well defined how patients were selected.

The major disadvantage of tests that aim to measure diffusion is that they become problematic when there is obstruction. This is considered a an important reason for the lack of correlation for DLco. The same accounts for Dlno. The fact that a correlation is found in this study does not exclude this problem. This should be discussed

In CF everything correlates with everything in a cross sectional setting. There is a wide range of PFT values and CT scores. Hence it is likely that a patient with a normal CT has (near) normal PFTs for a patient with severely abnormal CT has substantial abnormal PFTs. Why an extra test is needed? Does it tell something we do not know. In the discussion possible advantages on the use of DLno over other tests should be discussed.

P4, para2
It is stated that patients with a history of recent exacerbations or marked functional deteriorations within the time interval between CT and PFT were excluded from the study. Please specify in more detail the criteria of in and
exclusions. How many of the patients had an RTE between CT and PFT's. Please define in detail what is meant by 'marked functional deteriorations'

P6, para 1
To my knowledge the max Brody score is 180 when air trapping is excluded. The maximal score of $6 \times 36 = 216$ can not be obtained since some combinations can not occur. Please specify.
Furthermore to do the correlations were the scores normalized on a 0-100% scale. Please do so since it will allow comparisons with other studies.

Page 3, last sentence 1st para
It is stated that 'Dlco plays only a minor role’. More correct is no role. To my knowledge there are no data to support its use

Page 3, last sentence 2nd para
However; 'its’ rate. Please change to: the reactivity of CO with red……………..

P5, final para
Please define explicitly whether the order in which the CTs were scored was randomized and specify which randomization system was used.

Discussion page8, 2nd para
DLco is a useful marker. Pelase change to DLco is not a useful marker.

For all comparisons it is best to make CT the independent variable and the PFts the dependent variable. This was done so in figure 1 and 2. Please change to this perspective throughout the manuscript

P9, 2nd para
Thickness of the pulmonary… please change to the volume of blood. The thickness is not of importance.

Strikingly, however a high correlation……. Delete the ‘in the range of 0.8’

P10, 2nd para
‘fairly stable course of their disease’. As discussed before it is a major weakness of this study that there was a very large window between CT and PFT. What the authors mean with stability be clearly defined

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.