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:** 15 July 2008

**Reviewer:** Gerald Zavorsky

**Reviewer’s report:**

Because I would like all my comments addressed, my comments are thus labeled “major compulsory revisions” to everything below:

**Major comments**

The authors correlated DLNO, DLCO and other lung function parameters to the extent of cystic fibrosis damage from CT scanning. They proposed that DLNO would be superior to DLCO for the quantification of structural changes in the lung. Since thin section CT is the method of choice for looking at morphological changes in CF patients, they used CT scanning to correlate with various lung function parameters. They showed that that DLNO and DLCO were correlated well with the CT score. I like this study!

I however would not agree with the statement that DLNO seemed more sensitive to detect CF compared to the DLCO. I would suggest deleting the second sentence in the conclusion section of the abstract. An r2 or 0.66 versus 0.56 is not statistically different from each other. The 95% CI interval for the R2 (see [http://www.danielsoper.com/statcalc/calc28.aspx](http://www.danielsoper.com/statcalc/calc28.aspx)) for both DLCO and DLNO overlap with each other so the DLNO and DLCO relationship with CT score are similar to one another.

**Methods**

Why was there an exclusion criterion of an interval of more than 3 yrs between CT and PFT testing? Why not 1 yr? or 2 yrs? Is there any data showing that CT or PFT results are stable only up to 3 yrs? I think the authors should research the stability of CT and PFT testing over the long term in CF patients and include a paragraph or two in their manuscript. Page 10 in their discussion where they refer to reference 6 is a good start. They should rewrite their first sentence on page 5 in their “CT examination and scoring” section of the manuscript about this to make it more clear. The authors should report the mean, SD and range of the time between the CT scan and the pulmonary function testing. Page 10 in your discussion where you refer to reference 6 is a good start.

What was the NO analyser used? The authors should report this.

Why did the authors express Dm as DLNO / 1.97 when more recent data (see their reference 18, page 77, second column and also in Table 6 from reference...
18) show that Dm is better reflected by DLNO/2.42?

As well reference 18 predicts DLNO based on a patient’s VA. It would be interesting to have a percent predicted DLNO based on the patient’s VA. Then that percent predicted should be compared to the percent predicted based on the patient’s height (Table 4 from reference 18). Compare the two percent predicteds using a paired t-test to see if there is a difference. Therefore these authors can discern whether the reduction in DLNO from CF patients is mostly based on gas exchange abnormalities or lung volume problems or both (see discussion on page 75, second column of Reference 18). Then this could be included in the discussion section as you touch upon the topic on page 9.

DLCO was corrected to the standard Hb concentration. Is there evidence to support that patients with CF have normal Hb values? Can these authors find a reference for this and then include it?

Results

What was the predicted VA in these 21 subjects? I think they should report % predicted VA. And then add this finding to your discussion section.

How many CF patients were below the lower limit of normal (LLN) for DLCO and DLNO? (See Reference 18). I think the authors should report that.

I also think the authors should report the DLNO to DLCO ratio in Table 2.

Page 6 last 4 lines on the page, please round the percent predicted to a whole number. Decimals are not needed for % predicted. Are the % predicted from references 16 to 18 all based on gender, age and height?

Discussion

Page 8, 4th line from the bottom, starting with “Remarkably…” as mentioned earlier, I would like this sentence deleted. An r2 or 0.66 versus 0.56 is not statistically different from each other. The 95% CI interval for the R2 (see http://www.danielsoper.com/statcalc/calc28.aspx) for both DLCO and DLNO overlap with each other so the DLNO and DLCO relationship with CT score are similar to one another.

Conclusion

Page 10 second line, remove “most”

Page 11, change to read …challenging question of whether the….

Tables

SD should be used instead of the SEM. Please change.

Table 2 the % predicted values should be placed in the table. Maybe three different columns should be made for the % predicted values given that there are
three different DLNO prediction equations

Table 2, for DLNO DLCO and Dm, one decimal place should be used only. For age and Vc round to the nearest whole number.

Table 3 should be combined with Table 2 to make one table. The percent predicted should be rounded to the nearest whole number.

Figure and figure legend

Also I rather that the authors report the “r2” rather than the “r”. As well the 95% CI interval for the r2 should be reported for both Figure 1 Panel A and B and Figure 2 panel A and B. A web-link is provided to help the authors with this: http://www.danielsoper.com/statcalc/calc28.aspx

The authors should report the regression equation for each figure.

Overall assessment

My overall assessment of this manuscript is “accept with revisions” provided all my comments are adhered to.

Sincerely,

Gerald Zavorsky

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare I have no competing interests