Reviewer’s report

Title: Automated Measurement of Heterogeneity in CT Images of Healthy and Diseased Rat Lungs using Variogram Analysis of an Octree Decomposition

Version: 1 Date: 26 July 2013

Reviewer: Andrew J Bierhals

Reviewer’s report:

Overall, this is a novel method for the analysis of emphysema. The manuscript, data analysis and technique described are very solid.

Major revision:
I do not have any major revisions. The variogram analysis of emphysema is well described in the manuscript and offers the potential for a complementary method to categorize and diagnosis emphysema -- particularly in the preclinical phase of the disease process.

The major concern I have is validating the severity of the emphysema determined with the variogram analysis with the pathologic/histologic analysis. The report does describe why this was not performed, but I believe statements and/or references as to why this is not needed would improve this already solid manuscript. Also, I would urge the authors to do a follow-up study that includes the histology.

Minor essential revisions:
Could the authors please review the ordering and numbering of the figures. The manuscript seems to start with Figure 2 in the text. I could not find a figure 1. Also, figure 1 I think is not needed.

Descretionary revision:
You may want to consider how the results change or if they change by adjusting the HU cutpoint for the definition of emphysema.

Overall, excellent manuscript.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
'I declare that I have no competing interests'