Reviewer’s report

Title: Nerve ablation after bronchial thermoplasty and sustained improvement in severe asthma

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Reviewer: Ynuk Bosse

Reviewer’s report:

Facciolongo et al. have followed 12 severe asthmatics undergoing bronchial thermoplasty (BT). The symptoms and lung function were monitored before and after BT with validated questionnaires and spirometry, respectively. They have also collected bronchial biopsies before and at different time-points after the procedures to study the structural and inflammatory changes caused by BT. In addition to the expected improvements in symptoms, the authors reported a decreased number of nerve fibers within the airway smooth muscle and the submucosa.

While the concept is intriguing and likely possible, the current prove provided by the authors relies exclusively on a subjective measure. Is it possible to measure the mRNA expression of a nerve-specific gene in some of these bronchial biopsies? A decrease of which pre- versus post-BT would provide a quantitative assessment that is purely objective.

4 additional papers have shown a decreased content of airway smooth muscle post-BT. These should be cited.

Chakir et al., 2014 in Annals ATS

Pretolani et al., 2014 in the Blue

Salem et al., 2016 in Annals ATS

Denner et al., 2015 in Annals ATS

It is not clear why the authors have not quantified the effect of BT on the airway smooth muscle content. Is it because bronchial biopsies are not adequate specimens to quantify the amount of airway smooth muscle around the airways (Bullone et al. 2014 in JAP)?

Why repeated measures ANOVAs have not been used for symptoms?

Page 6, line 13. Student's unpaired t-test is not a posteriori test for ANOVAs.

How a Friedman test can be used when data are missing at T12 (n = 7)?

The quality of the figure 1 and 2 is poor. Neither the title nor the units are displayed on the y-axis for each graph presented in Figure 2.
Page 3, line 9. Pretolani is the first author on this paper. It needs to be referred to accordingly.

Page 6, lines 14-15. This sentence is unreadable.

Page 17, Line 16. The authors meant over 18 years I suppose (age > 18 years).

Table 4. RV not VR

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Unable to assess

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Acceptable

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