I found the concept and research question of the manuscript very interesting, and would like to recommend it for publication with some comments. I am interested in lung branch formation in humans, and while I have found mathematical models that predict branching patterns, I had yet to read an article describing the transition zone between the bronchial and alveolar zones and its predictive location across the mammalian species. As a disclaimer, I am not able to fully follow the mathematical derivations and vet for the models presented.

The authors propose a generalized model across mammals to predict the location of a 'transition zone' between convective and diffusive transport areas in the lung. While several models have proposed predictions of branching structures, models have not been applied to predict where this transition occurs taking into account the energetic cost of ventilation according to mass and metabolic rates across mammalian species. In the manuscript, two models were developed for separate purposes: (1) to estimate O2 capture in lungs and (2) to estimate ventilation costs. Authors conclude that allometric scaling laws across species for breathing rates and tidal volumes minimize mechanical energy used. This study adds to the work that argues that mammalian tidal volumes and breathing rates are dependent upon a select number of geometrical characteristics.

The introduction clearly explains the two functional zones of the lung bronchial tree and respiratory zones, and what has been found in recent literature regarding the transition zone between the two in humans. The authors build up to the question of expanding across mammalian species in a natural and cohesive manner. The potential for the impact of such a model is explained -- a successful model would be a powerful tool to predict breathing rates at maximal exercise of various mammals, for example. I would be curious to know how we might see applications in obtaining accurate predictions for this. Who would want to use it and why?

My main concern is with the oversimplification of branching patterns in the lungs. Although this is addressed in discussion, authors may want to consider bringing it up sooner. Lung branching in the mouse is well known to have three modes of branching: domain, planar, and orthogonal branching as described by Metzger et al. 2008, with two phases of a stereotypic pattern layout followed by a series of bifurcations. Lung branching has been described as 'volume filling' -- which is not best described by continuous rounds of bifurcations at the same angle. Early stereotypic branching allows for a final pattern with many alveoli present close to the trachea. This may suggest a larger respiratory zone reserve than the one considered here. Figure 1 describes a branching pattern with alveoli present only on the outer surfaces. I would also be interested in seeing what branching generations the model predicts in well-studied species (ie. it is known that mice have 13-17 branching generations, and humans 17-23).

I have noted several minor improvements to the writing:

- 2nd paragraph of Discussion (page 7):
  Delete first "the" and replace the second "the" with "specifically", "especially" or "such as"
  "This raises the question about the influence of the other respiratory gas, the carbon dioxide." → "This raises the question about the influence of other respiratory gases, and specifically, carbon dioxide."
- 6th paragraph of Discussion (page 9):
  Replace "Actually" with "Instead"
  "Actually, it predicts that small mammals should exhibit a breathing rate at…" → "Instead, it predicts that small mammals should exhibit a breathing rate at…"
- Final sentence:
  Bring "more specifically" after "these configurations."

“Our model could be used to study more specifically these configurations” →
“Our model could be used to study these configurations more specifically”