Background – Targeted lung denervation (TLD) utilizes radiofrequency (RF) ablation within the main bronchi to disrupt nerve inputs to the lungs.

- Parasympathetic motor nerve tone in COPD
  - Patients with COPD have increased parasympathetic tone in the lungs
- Anticholinergics decrease parasympathetic tone and reduce resistance to airflow in patients with COPD
- Targeted lung denervation (TLD)
  - A novel one-time cholinergic bronchospasm procedure developed by Nuvaira Inc.
  - Utilizes RF ablation within the main bronchi to disrupt parasympathetic motor nerve input to the lungs

RF catheter is designed to achieve nerve disruption with minimal effects to the airway surface and peribronchial structures.

- The Nuvaira™ Dual Cooled RF Catheter:
  - Provides conductive cooling to the airway surface during RF energy delivery
  - Maintains the integrity of the airway mucosa during TLD
  - Targets bronchial nerve fasciculi at depth from the airway surface

Aim: To determine the effect of lung denervation on pulmonary resistance in healthy sheep.

Methods: Following IACUC approval, 3 sheep underwent circumferential ablation of both main bronchi using a lung denervation system (Nuvaira™, Inc., USA). All sheep were mixed breed and weighed 47-51 Kg. Prior to and following TLD therapy, each animal underwent a series of pulmonary resistance measurements using a custom built forced oscillometry system. Atropine was utilized as a positive control to demonstrate bronchodilation prior to TLD.

Aim:
- To determine the effect of lung denervation on pulmonary resistance in healthy sheep.

Results: The effect of TLD therapy was evident in all three animals. On average, the airway resistance decreased by 27% (1.34 cm H2O/L/sec) and 30% (1.21 cm H2O/L/sec) in response to the peak effect of atroine and post-TLD therapy, respectively. The effect from TLD was maintained at 80 min post treatment while the effect of atropine was sustained over the same time frame.

Conclusion: Healthy sheep subjected to TLD demonstrated decreased airway resistance comparable to the peak effect of atropine.

Hypothosis – TLD with the Nuvaira™ Lung Denervation System in sheep disrupts parasympathetic input to the lungs decreasing pulmonary resistance.

Methods – 3 sheep underwent circumferential ablation of both main bronchi using a lung denervation system (Nuvaira™, Inc., USA).

- Each bronchus of 3 sheep underwent TLD with the Nuvaira™ System
  - The study was conducted under the guidance of an Institutional Animal Care and Use Committee in accordance with the study facility SOP and Animal Welfare Act of 1966
  - Each bronchus (n = 6) underwent 8 sequential RF activations evenly spaced around the circumference of the airway (octants)
  - Prior to and following TLD therapy, each animal underwent a series of pulmonary resistance measurements using a custom built forced oscillometry system.
  - Atropine was utilized as a positive control to demonstrate bronchodilation prior to TLD.

Pulmonary Resistance Measurement

Results – Atropine caused a transient 26% peak reduction in pulmonary resistance that normalized after 25min.

Conclusion – TLD treatment induces bronchodilation through nerve disruption that is sustained and comparable in magnitude to the anticholinergic effect produced by atropine.