

Targeted lung denervation in the healthy sheep model – A potential treatment for COPD

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Introduction: Targeted lung denervation (TLD), a bronchoscopic procedure to disrupt pulmonary parasympathetic inputs, may be an important treatment for COPD. Holaira has developed a novel radiofrequency ablation catheter with dual cooled design to facilitate ablation of bronchial branches of the vagal nerve while minimizing epithelial effects.

Aim: To determine the ability to durably denervate the lung, protect the airway surface, and minimize damage to peribronchial structures.

Methods: 28 sheep underwent circumferential ablation (20W) of both main bronchi with simultaneous balloon surface cooling using a lung denervation system (Holaira, Inc., USA). Animals were followed over an extended time course (30, 90, 180, 365, and 640 days post procedure). At each time point, lung denervation (axonal staining in bronchial nerves), surface protection at the treatment site (histopathology of bronchial epithelium), and effect on peribronchial structures near the treatment site (histopathology of bronchial cartilage, vasculature, smooth muscle, alveolar parenchyma, and esophagus) were quantified.

Results: No adverse clinical effects were seen in any sheep. Axonal staining was consistently decreased 60% at 30 days after TLD and motor axon staining was decreased by 75% out to 640 days. All treated airways exhibited 100% epithelial integrity (56 of 56 treated airways). Effect to peribronchial structures was strictly limited to immediately adjacent lung tissue. Tissue 1cm proximal and distal to the treatment was normal, and the esophagus was unaffected.

Conclusions: TLD treatment durably denervates the lung while protecting the bronchial epithelium and minimizing effects on peribronchial structures.