

Targeted lung denervation; an evaluation of power dose effect

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Introduction: Targeted lung denervation (TLD) is a bronchoscopic procedure developed to relieve obstructive airways disease by disrupting pulmonary vagal parasympathetic inputs.

Aim: Define dose effect of TLD.

Methods: Following IACUC approval, 26 sheep underwent TLD using a second-generation lung denervation system (Nuvaira, Inc., USA) at multiple powers (30, 34, 36, and 38+ W). Each animal's airways underwent bronchoscopic evaluation and semiquantitative histologic evaluation for safety and efficacy at 30 and 90 days post TLD.

Results: There were no animal deaths or significant clinical observations. The effect of TLD was largely undetectable under gross and bronchoscopic inspection except at 38+W. Histologically, the targeted treatment zone at all doses consisted of a layer of unaffected tissue encompassing the epithelium, lamina propria, and smooth muscle layers of the airway wall, with a ring of well-organized fibrosis in the outer layer of the airway wall. This fibrosis extends into surrounding adventia encasing and obliterating nerve fascicles. Bronchial cartilage effects were limited to the zone and consisted of matrix changes, atrophy, and limited necrosis. Fibroplasia extended up to, but spared, the outer wall of the pulmonary arteries and veins with minimal fibrosis observed in the outer vessel wall at two treatment sites. Tissue proximal and distal to the zone were normal and absent of any treatment effect. Scoring of axonal staining demonstrated similar disruption of nerves at all treatment doses.

Conclusions: The current study demonstrates that over the dose range tested, the system safely created a band of fibroplasia surrounding the sheep airway that disrupted axons in bronchial nerve fascicles.