A multicenter trial of an intrabronchial valve for treatment of severe emphysema

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The members of the Spiration research group are listed in Appendix 1.

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Objectives: Minimally invasive endoscopic treatment of emphysema could provide palliation with less risk than lung volume reduction surgery and offer therapy to patients currently not considered for lung volume reduction surgery. The Intrabronchial Valve is used to block bronchial airflow in the most emphysematous areas of lung.

Methods: Patients with severe chronic obstructive pulmonary disease and heterogeneous upper lobe–predominant emphysema were eligible. Patients underwent flexible bronchoscopic placement of valves into segmental or subsegmental airways in both upper lobes. Outcomes assessed over a minimum of 6 months of follow-up included the safety, feasibility, tolerance, and success of valve placement; health-related quality of life; exercise capacity; pulmonary function; and gas exchange.

Results: Five centers treated 30 patients. Patient follow-up ranged from 1 to 12 months. A mean of 6.1 valves were placed per patient. Valves were positioned by means of flexible bronchoscopy in 99% of desired airways, and the procedure duration ranged from 15 to 125 minutes (mean, 65 minutes). Hospital discharge occurred within 2 days in 27 of 30 patients. There were no deaths or episodes of valve migration, tissue erosion, or significant bleeding. Eighty-three percent of patients had no adverse events judged probably or definitely related to the device. Patients experienced significant improvement in health-related quality of life, although the physiologic and exercise outcomes did not show statistically significant improvements.

Conclusions: These first multicenter results with the Intrabronchial Valve demonstrate significant improvements in health-related quality of life and acceptable safety, ease of use, and procedural complication rates. The valve might be a safer and less-invasive alternative to surgical therapy for patients with severe emphysema.

Emphysema affects 2 to 3 million persons in the United States and is characterized by progressive deterioration in pulmonary function, with exercise limitation, disabling dyspnea, and an inexorable decrease in quality of life. Until recently, surgical palliation of the symptoms of emphysema was only used for the very small subset of patients with giant bullae. Lung transplantation was introduced as an option for patients with end-stage emphysema in the 1980s, but it is only offered to the most severely ill patients who have minimal comorbidity and

Abbreviations and Acronyms
COPD = chronic obstructive pulmonary disease
IBV = Intrabronchial Valve
LVRS = lung volume reduction surgery
NETT = National Emphysema Treatment Trial
SGRQ = St George's Respiratory Questionnaire

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younger age. The number of transplantations performed is further limited by a shortage of lung donors, with only approximately 400 patients with emphysema per year (0.013%) undergoing transplantation.[1] Lung volume reduction surgery (LVRS) was reintroduced in the early 1990s and has had its efficacy investigated more thoroughly than perhaps any other new surgical procedure. LVRS improves pulmonary function, exercise capacity, and quality of life in selected patients with severe chronic obstructive pulmonary disease (COPD) and emphysema, but it has demonstrated major limitations.[2] First, the benefit of LVRS is limited to narrow subsets of patients with certain patterns of emphysema and with minimal comorbidity.[2] Second, patients undergoing LVRS have significant risk of morbidity that can extend the period of convalescence before they can realize the desired clinical improvement or that might prevent benefit from LVRS at all.[3]

The goal for future developments in the treatment of advanced emphysema would be to provide similar benefit as LVRS, with less risk, shorter recovery, and decreased cost. Endobronchial occlusion with a plug or valve might be able to produce targeted areas of atelectasis and subsequent lung reduction with similar physiologic and functional outcomes to LVRS. Alternatively, valve occlusion of the airways might have effects that differ from LVRS, such as the ability to decrease dynamic hyperinflation, work of breathing, and dyspnea with exertion. The Intrabronchial Valve (IBV; Spiration, Inc, Redmond, Wash) is a novel implantable device designed as a one-way valve that is placed by means of flexible fiberoptic bronchoscopy. The IBV obstructs airflow into targeted bronchopulmonary segments and in unpublished animal model studies appears to allow drainage of distal air and mucus. This report describes the initial pilot human study results with the IBV to determine feasibility and safety data before proceeding to a larger pivotal clinical trial.

Materials and Methods

This prospective, open-enrollment, multicenter cohort study enrolled patients with heterogeneous, upper lobe–predominant emphysema, and severe COPD (Table E1). Patients excluded from the trial were those already accepted and listed for LVRS or lung transplantation, those defined as high risk within the National Emphysema Treatment Trial (NETT),[4] those having a significant bronchospasm, or those with chronic bronchitis and heavy sputum production. Screening studies were similar to those used by the NETT,[5] including baseline physiologic, radiologic, and quality-of-life testing. Patients were required to fulfill a pulmonary rehabilitation program or complete more than 140 m in a 6-minute walk test. The clinical protocol was reviewed and approved by each investigating site's institutional review board and monitored by an oversight data safety monitoring board. All patients provided informed consent for the procedures, data collection, and participation in the clinical trial.

The IBV is an implantable device designed for placement in the segmental or subsegmental bronchi by means of flexible bronchoscopy (Figure E1). The valve is made of a nitinol framework. The valve's 5 distal anchors provide stability and allow distal seating of the valve into the airway without perforation. The proximal portion is made up of 6 support struts that are covered by a synthetic polyurethane polymer. The membrane-covered struts expand radially and form an umbrella shape that allows conformation and sealing to the airways with minimal pressure on the mucosa. The valve is designed to limit distal airflow, yet the membrane and support struts should allow air and mucus to flow out of the occluded segment by compressing the umbrella. The valve design includes a proximal center rod that allows early repositioning or removal.

Patients underwent general anesthesia with endotracheal intubation. Therapy generally consisted of bilateral occlusion of all upper lobe segments except for the lingula, with placement of valves into segmental airways, subsegmental airways, or both to occlude all planned segments. Airways were sequentially sized with a calibrated balloon to determine valve size. Available valve diameter sizes were 4, 5, 6, and 7 mm. For segments with a diameter of greater than 7 mm, subsegmental orifices were measured to define subsegmental valve size.

The IBV was deployed by means of flexible bronchoscopy with 2 different delivery systems. The direct-load system provided a loading kit that allowed the valve to be compressed and loaded retrograde into the 2-mm working channel of the bronchoscope (Figure E2, *A*). In the direct-load configuration the tip of the bronchoscope was inserted into the orifice to be occluded, and the tip of the scope was positioned at the desired depth of the valve anchors. The IBV deployment tool was used to advance the valve out of the working channel. When the anchor tips extruded and contacted the bronchial wall, the bronchoscope was withdrawn while continuing to deploy the valve until it was fully delivered out of the bronchoscope.

The catheter-load system compressed the valve into a 2.2-mm flexible delivery catheter with an integral deployment rod (Figure E2, *B*). The catheter was then placed through the working channel (≥2.6 mm) of the flexible bronchoscope and directed into the targeted airway. The valve was visualized through the clear sheath of the delivery catheter and positioned so that the top of the valve membrane and struts was at the level of the desired position in the airway. The valve was then deployed, the position was assessed, and adjustments were made as necessary. The catheter shaft was revised for the last 8 patients to prevent stretching and nondeployment of the valve. Before the catheter revision, the direct-load technique was the dominant method used.

Valves were deployed in all planned segments or subsegments, followed by a final visual inspection. The patient was then extu-