



**Australian Government**  
**Department of Health and Ageing**



**Horizon Scanning Technology**  
**Prioritising Summary**  
**Intrabronchial valve for chronic obstructive  
pulmonary disease**

**May 2007**



**Australian  
Safety  
and Efficacy  
Register  
of New  
Interventional  
Procedures -  
Surgical**



**Royal Australasian  
College of Surgeons**

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Enquiries about the content of the report should be directed to:

HealthPACT Secretariat  
Department of Health and Ageing  
MDP 106  
GPO Box 9848  
Canberra ACT 2606  
AUSTRALIA

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

This Horizon scanning prioritising summary was prepared by Mr. Luis Zamora from the Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

# PRIORITISING SUMMARY

**REGISTER ID:** S000041

**NAME OF TECHNOLOGY:** SPIRATION INC. INTRABRONCHIAL VALVE

**PURPOSE AND TARGET GROUP:** LUNG FUNCTION IMPROVEMENT AND SYMPTOM RELIEF IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

## STAGE OF DEVELOPMENT (IN AUSTRALIA):

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established  |
| <input type="checkbox"/> Experimental             | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational          | <input type="checkbox"/> Should be taken out of use   |
| <input type="checkbox"/> Nearly established       |   |

## AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- |   |             |     |
|---|-------------|-----|
| <input type="checkbox"/> Yes            | ARTG number | N/A |
| <input checked="" type="checkbox"/> No  |             |     |
| <input type="checkbox"/> Not applicable |             |     |

## INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Canada	✓		
Europe	✓		
United States	✓		

## IMPACT SUMMARY:

Spiration Inc. (Washington, United States), provides the intrabronchial valve (IBV) with the aim of improving lung function and symptom relief in patients suffering chronic obstructive pulmonary disease. The technology is current under investigation in Canada, Europe and the United States.

## **BACKGROUND**

Chronic obstructive pulmonary diseases (COPDs) are a group of diseases, which cause progressive, irreversible lung damage and include emphysema, asthma and chronic bronchitis (Kleinschmidt 2007). COPDs are characterised by airflow obstruction and a ratio of forced expiratory volume over 1 second ( $FEV_1$ ) to forced vital capacity (FVC) of  $<0.7$  and  $FEV_1$  50% to 80% of the predicted value (Devereux 2006).

COPDs are most often associated with cigarette smoking although other airborne irritants including coal dust, asbestos and solvents have also been associated with it (Devereux 2006). It has been estimated that between 80% and 90% of all COPD related deaths are associated with cigarette smoking (US Department of Health and Human Services 2004). The symptoms most often associated with COPD include dyspnea (shortness of breath), sputum (mucus) production, coughing, wheezing and chest tightness (National Heart Blood and Lung Institute 2006).

Emphysema has been identified as the most serious COPD (Kleinschmidt 2007). Emphysema is a condition characterised by abnormal permanent enlargement of air spaces accompanied by a loss of elasticity and eventual breaking of the alveoli (Sharma 2006). As a result, air becomes trapped in the enlarged alveoli leading to an inadequate exchange of oxygen and carbon dioxide. Sufferers therefore experience difficulty expelling air from their lungs. Because the disease develops gradually, symptoms gradually worsen as the disease develops (Sharma 2006). Over time patients may even have difficulty breathing while lying down.

Treatment of emphysema as well as other COPDs is targeted at the management of symptoms (National Heart Blood and Lung Institute 2006). Lung volume reduction surgery (LVRS) is currently the standard surgical treatment for patients with severe emphysema. The surgery removes the most damaged areas of the lung helping to reduce hyperinflation of the lungs relieving symptoms (Fabbri et al. 2005). Unfortunately LVRS is only an option for a small subset of patients with minimal co-morbidities (National Emphysema Treatment Trial Group 2003). Lung transplantation is another surgical option. Unfortunately due to the shortage of lung donors only very few patients are offered this option (Wood et al. 2007).

The Intrabronchial Valve by Spiration Inc. is an implantable one-way valve designed to obstruct air-flow into targeted bronchopulmonary segments thus redirecting airflow to healthier areas of the lung, improving lung function and treating symptoms associated with COPDs. The IBV is designed for placement into the segmental and sub-segmental bronchi and can be placed by means of flexible fiberoptic bronchoscopy.

## **CLINICAL NEED AND BURDEN OF DISEASE**

In Australia, during 2003, COPD was recorded as the underlying cause of death in 5,378 people (4% of all Australian deaths) and as an associated cause of death in 7,208 people (AIHW 2005). In the 2001 Australian National Health Survey (NHS), 3.5% of Australians reported having bronchitis or emphysema (AIHW 2005b). However this figure may have underestimated the true prevalence of COPD among the Australian population given that COPD is not diagnosed until it begins to affect a person's lifestyle and is already moderately advanced (AIHW 2005b).

## **DIFFUSION**

The IBV is currently only approved for investigational use only in the United States, Europe and Canada. The device is not available in Australia.

## COMPARATORS

Surgical treatments for emphysema (Kleinschmidt 2007):

- Lung transplantation
- Lung volume reduction surgery
- Bullectomy

## SAFETY AND EFFECTIVENESS ISSUES

Wood et al. have reported on the first and to date the only human trial using the IBV (Wood et al. 2007). The study, a prospective, multi-centre trial, enrolled 30 patients suffering from heterogenous, upper lobe-predominant emphysema and severe COPD. The patients included in this study represent a small subset of patients suffering COPDs with severe symptoms. All patients experienced severe to very severe airflow obstruction, with air trapping, thoracic hyperinflation and reduced diffusing capacity of lung for carbon monoxide value.

The IBV was implanted into segmental, sub-segmental or both segmental and sub-segmental airways under general anaesthesia with the aim of bilateral occlusion of all upper lobe segments (except for the lingula). Delivery of the IBV was performed using flexible bronchoscopy and either a direct load system (provided in loading kit, n = 22) or a catheter based load system (n = 8). The average time for the implantation procedure was 65 minutes using the direct load system and 41 minutes using the catheter based system. A total of 184 valves were implanted in patients during this initial round of procedures with the number of implanted valves rising to 194 following completion of a one month bronchoscopy procedure (mean number of valves per patient was 6.5).

Overall implantation of the IBV was successful with the exception of two sites (anterior sub-segments of the upper lobes of each lung) during the initial procedures where the angle did not allow scope entry for direct load placement. It was not reported whether these two sites occurred in the same or different patients. Nevertheless implantation of the sites was successfully achieved during the second round of implantations after the one month bronchoscopy. At the one month bronchoscopy, revision surgery was performed in 17 patients, which included the removal of eight valves, replacement of 16 valves and placement of an additional 15 valves in new segments or sub-segments. The revisions were performed based on visual judgement that valves had become angulated or moved too distal in an airway, resulting in incomplete contact between the valve and an airway wall.

Patients were discharged according to protocol specifications (median hospital stay: two days). Only two patients required hospitalisation greater than three days. In one patient the extended hospitalisation was due to delays in the patient's transportation needs while in the other chest pain, wheezing and acute respiratory distress resulting in cardiopulmonary arrest led to a 33 day admission. This patient survived but suffered a second arrest and experienced nosocomial pneumonia. At 21 days after the initial procedure all valves were removed (reasons for removal not stated). Follow-up at eight months indicated a return to baseline with no adverse events from valve implantation.

There were four withdrawals during the study period. One patient withdrew just prior to six month evaluation while another withdrew at eight months. It was not stated whether these patients underwent valve removal. The other two withdrew at seven and nine months and underwent valve removal for anticipated LVRS. Therefore at six months data for 28 patients was available.

Seven patients (48 valves) underwent late valve removal during the study period. This included the two patients for anticipated LVRS, two patients with pneumonia in area of the valves (n = 2), and non-responders who requested removal at 3, 5 and 8 months respectively. In one of the patients who underwent valve removal for anticipated LVRS, one valve was not removed due to inadequate visualisation and difficult access.

A panel of experts, investigators as well as personnel from Spiration Inc. determined that no adverse events were definitely attributed to implantation of the valves. Alternative methods of describing adverse events including adverse events probably related, adverse events possibly related and adverse events definitely not related to valve implantation were reported. Under these headings, six events in five patients were judged to be possibly related, 20 events in 12 patients were judged to be probably not related and 50 events were judged definitely not related to valve implantation. Various complications and thoracic events which occurred during peri-procedure, first 30 days from implantation and 30 to 180 days from implantation were reported (Table 1) however it was not stated which complications were attributed to implantation of the IBV.

**Table 1: Complications and thoracic events reported by Wood et. al (2007)**

Period	Complications	No. of events
Peri-procedure	Bronchospasm	4
	Arrythmia, cardiovascular	6
	P <sub>a</sub> CO <sub>2</sub> retained	2
	Dyspnea	1
	Hemoptysis	1
First 30 days	COPD flare	4
	Bronchitis	3
	Dyspnea	3
	Thorax pain	2
	Hemoptysis	1
	Pneumonia	4
30 to 180 days	COPD flare	4
	Bronchitis	4
	Dyspnea	3
	Thorax pain	1
	Hemoptysis	1

A variety of measures of quality of life, lung function, gas exchange and exercise tolerance before and after valve implantation were used to determine efficacy of the IBV. According to the authors, the only consistent measure of efficacy was seen by the St George's Respiratory Questionnaire (SGRQ) which measured the impact on overall health, daily life and perceived well being. Using this instrument significant improvements in the SGRQ scores were observed at one month (p < 0.0001), three months (p = 0.01) and six months (p = 0.05) after valve implantation. However, given the subjective nature of the SGRQ and the low number of patients involved in the study the possibility of a placebo effect cannot be ignored and it is therefore not possible to derive a definitive conclusion regarding the efficacy of the IBV.

## **COST IMPACT**

A search of the published literature and website of the IBV manufacturer (Spiration Inc.; Washington, United States) did not reveal the cost of the IBV or procedure required to implant the device. Table 2 shows the Medicare Benefits Schedule of fees related to the treatment of COPD in Australia.

**Table 2: Medical Benefits Schedule of fees related to the treatment of COPD (Department of Health and Ageing 2007)**

<b>Category</b>	<b>Item Number</b>	<b>Benefit (AUD)</b>	<b>Number of Claims (July 2005 to June 2006)</b>
Wedge resection	38440	\$1,073.70	872
Thoracotomy and lung resection for congenital cystadenomatoid malformation or congenital lobar emphysema	43861	\$1,473.90	4

### **ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS**

No issues were identified from the retrieved material.

### **OTHER ISSUES**

No issues were identified from the retrieved material.

### **RECOMMENDATION:**

The evidence currently available on the IBV valve is limited to one non-comparative study of 30 patients. Safety was difficult to assess in this severely affected patient population, however it is of note that one patient experienced a peri-operative event that led to cardiopulmonary arrest and 33 day hospital admission and seven patients required valve removal. Efficacy was demonstrated by improvements in quality of life from baseline in this small select sample of patients with COPD and heterogeneous upper lobe-predominant emphysema was. Taking into consideration that the IBV is designed to improve lung function in COPD patients, that the patient sample presented is not representative of the wide spectrum of COPD patients and that further safety data are required. It is recommended that this technology is archived.

### **SOURCES OF FURTHER INFORMATION:**

Spiration Inc. is currently in the process of conducting a non-randomised safety study of the IBV in patients with severe emphysema in the United States. The study has an expected total enrolment of 115 patients and is expected to be completed by September 2007 (ClinicalTrials.gov identifier: NCT00145548). The company is also sponsoring clinical studies of the IBV in Europe and Canada.

### **LIST OF STUDIES INCLUDED**

Total number of studies            1  
Level IV intervention evidence

### **SEARCH CRITERIA TO BE USED**

COPD  
Chronic obstructive pulmonary disease  
Emphysema  
Spiration  
IBV  
Intrabronchial valve  
Intra-bronchial valve

Valve  
Lung valve

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