**Emerging Technology List**  
**PERCUTANEOUS HEART VALVE REPLACEMENT**  

**Technology:** Percutaneous heart valve replacement is an interventional radiology procedure involving the insertion of an artificial heart valve using a catheter, rather than through open heart surgery.

**Manufacturer:** Several companies are developing devices for percutaneous heart valve replacement. The Cribier-Edwards percutaneous aortic heart valve (Edwards Lifesciences Corporation, Irvine, CA) and the ReValving™ System (CoreValve, S.A. Paris, France) are being used in human trials. Other companies reported to be working in this area include Heart Leaflet Technologies, Inc.; Medtronic, Inc.; and Boston Scientific.1 Percutaneous pulmonary valve replacement has been investigated by Dr. Philippe Bonhoeffer *et al.*, using devices that are already on the market.

**Purpose:** A common valvular disease in adults is calcification and stenosis (narrowing) of the valve – a condition often associated with aging. Another type of malfunction involves leakage (regurgitation) of the valve. Heart valve replacement, which may be used to treat severe valvular disease, involves open heart surgery.

About 4,000 to 4,500 heart valve replacements are performed in Canada annually (Dr. Philippe Pibarot, Department of Medicine, Laval University, Sainte Foy, QC: personal communication, 2005 Mar 21).2 Many individuals with valvular disease are considered to be at high risk or ineligible for this surgery because of additional health conditions. According to Dr. Philippe Pibarot, Canada Research Chair in Valvular Heart Diseases, about 3% to 5% of Canadian patients (100 to 150 Canadians) with severe aortic stenosis, who undergo aortic valve replacement, are high risk patients because of their depressed left ventricular function and other comorbidities. These patients might eventually benefit from a less invasive procedure. In addition, another 100 to 150 Canadian patients who would be considered ineligible for aortic heart valve replacement surgery might be eligible for percutaneous valve replacement. For many patients in this group, the procedure may be considered palliative – it would improve quality of life rather than increase life expectancy. Percutaneous heart valve replacement may also be useful for pulmonary valve replacement in children and young adults with congenital heart diseases (Dr. Philippe Pibarot: personal communication, 2005 Mar 21).

A UK Heart Valve Registry study of octogenarians who underwent open heart surgery for aortic heart valve replacement found a mortality rate of 6.6% at one month and 11% at one year. At one month follow-up, the total mortality rate for all age groups in the registry was 4.3%.3

**Current Regulatory Status:** Heart valves that are intended for percutaneous implantation are in development and clinical trials in humans have only begun recently. These devices are not yet licensed by Health Canada or by the US Food and Drug Administration (FDA). Use of the percutaneous device in Canada is possible on compassionate grounds through Health Canada’s Special Access Programme.
Description: In percutaneous heart valve replacement, an artificial valve and stent device are inserted through a catheter into the diseased heart valve under fluoroscopic guidance. The device is fitted in the native stenotic heart valve (which is not removed), by an interventional cardiologist. Unlike traditional valve replacement surgery, the percutaneous approach does not require open heart surgery or the use of extracorporeal circulation (heart-lung bypass).

The percutaneous approach is technically complex and accurate positioning of the replacement valve is more difficult than with open heart surgery. The first percutaneous aortic heart valve replacement in North America was performed by Dr. John Webb, at St. Paul’s Hospital in Vancouver, using the Cribier-Edwards percutaneous aortic valve. Percutaneous aortic heart valve replacement at St. Paul’s Hospital, began in February 2005 (Dr. John Webb, St. Paul’s Hospital, Vancouver: personal communication, 2005 Mar 23). Dr. Webb has performed the procedure on several patients in Vancouver using a retrograde, transaortic approach with a special delivery system. According to Dr. Webb, this approach is less complex than the technique used by Dr. William O’Neill and colleagues, for the first US patient (Dr. John Webb: personal communication, 2005 Mar 23). Dr. William O’Neill reported that the procedure was “the most complicated procedure I’ve ever done.” Three cardiologists were needed to thread the guidewires, balloon catheters, temporary pacemaker and stent containing the valve through the femoral vein to the aorta.4

Cost: Information on the cost of percutaneous heart valve replacement devices is unavailable. No studies of the hospital costs (for staffing, catheterization, laboratory work or length of stay) associated with this procedure were identified.

Evidence: There have been no published reports of controlled clinical trials of percutaneous heart valve replacement. The evidence comes from case reports. Similarly, there have been no systematic reviews of the safety or effectiveness of these devices.

Work on percutaneous aortic valve replacement has been led by Dr. Alain Cribier and colleagues.5-10 Their first case report, of a 57-year-old patient who received the treatment in Europe, was published in 2002. Although the heart valve procedure was successful, the patient died 17 weeks later from an infection after amputation due to severe leg ischemia.5,7

Initially designed by Percutaneous Valve Technologies, this device is now being developed by Edwards Lifesciences, which has US FDA approval for a single centre feasibility trial involving 20 patients who are considered to be at high risk for conventional valve replacement surgery. The patients will be randomly selected to receive percutaneous aortic valve replacement or balloon aortic valvuloplasty. In March 2005, the first patient in the trial underwent the procedure at the Beaumont Hospital in Michigan. According to a news report, the 76-year-old patient was discharged from hospital three days after the procedure.4 If the initial study results warrant, a second multi-centre trial of 40 patients will be undertaken.11 In the REVIVAL
In 2004, Cribier et al. reported their early experiences with percutaneous aortic valve replacement using a trileaflet equine tissue valve inside a stainless steel stent. The six patients (including the 57-year-old patient, described previously, who received an earlier device composed of bovine tissue) were considered to be ineligible for surgery because of severe aortic stenosis and comorbid conditions. The procedure was performed under local anesthesia with mild sedation. One patient died as a result of device migration during the procedure. Three other patients died of unrelated causes in the weeks after valve replacement. The two remaining patients were discharged from hospital on days 12 and 15, with no signs of heart failure at eight weeks follow-up.9

The most recent paper by Cribier et al. is a report about eight patients with severe aortic stenosis who were ineligible for valve replacement surgery because of hemodynamic instability and severe comorbidities. The patients, six women and two men, ranged in age from 77 to 88 years (mean age 82.6±3.3 years). All patients were rated as New York Heart Association class IV, with two patients in cardiogenic shock. An antegrade transseptal approach was used in six patients and a retrograde arterial approach was used in two patients. The aortic heart valve was percutaneously implanted in all patients. Doppler imaging was used to monitor left ventricular function before and after the procedure. The investigators reported that there was significant improvement in patients’ global and regional left ventricular function 24 hours after implantation. At one month follow-up, three patients had died. The causes of death were not described.10

In a 2004 lecture to the Japanese Circulation Society, Dr. Cribier described his experiences with the first 20 patients who underwent percutaneous aortic valve replacement. An antegrade approach was used for 13 patients (procedure time of approximately 90 minutes, fluoroscopy time of approximately 25 minutes) and a retrograde approach was used in the other seven patients (approximate procedure time of 60 minutes, fluoroscopy time of 20 minutes). Successful implantation was achieved in 17 patients. Complications related to the procedure included one stroke when the aortic valve was crossed with the guidewire; one right ventricular perforation; one death during pre-dilation of the valve; and one death after the implantation procedure and removal of the right femoral artery sheath.13

A July 2004 news release announced the first use of the ReValving aortic valve replacement system (CoreValve, S.A.), in India, in a 62-year-old patient with severe aortic calcification and stenosis. CoreValve reported that this was part of a phase 1 feasibility study of 21 patients in India.14 The interventional cardiologists involved in performing the procedure, Dr. Eberhard Grube and Dr. Jean-Claude Laborde, report-
ed that the “patient’s blood flow was restored to normal almost immediately, and his heart function…improved dramatically. The results show a perfect implantation, absence of transvalvular gradient, and no significant valvular regurgitation, either centrovalvular or paravalvular.”15 A trial of the ReValving system is underway with 20 patients at The Heart Center in Siegburg, Germany. The first patient in the trial, a 73-year-old female, underwent the procedure in February 2005. According to a CoreValve press release, the “patient improved immediately following the implant – her cardiac output increased from 1.2 liters per minute to 2.5 liters per minute, and her left ventricular ejection fracture improved remarkably – from 45 to 72 percent – immediately following the ReValving procedure.”16

Bonhoeffer, Boudjemline and colleagues have published several papers describing their experience with percutaneous pulmonary valve replacement in the treatment of pulmonary regurgitation.17-22 These investigators used a trileaflet bovine jugular vein valve (VenPro Corporation) sutured into a vascular stent with a balloon catheter delivery system (NuMed, Inc.), while patients were under general anesthesia. In 2003, the authors reported that implantation was accomplished in all 14 patients (11 children and three adults). Obstruction due to blood flowing between the valve and the stent occurred in three patients. In two patients, a second valve was implanted and the problem resolved, but the third patient required surgery after seven weeks because of further obstruction. In one patient, the valve was explanted a year later due to endocarditis (infection) after dental treatment without antibiotic prophylaxis. The stents fractured in two patients, though their valves continued to function. The authors reported that the “clinical state of all patients improved during follow-up.”20 Khambadkone and Bonhoeffer reported that 12 other patients successfully underwent the procedure at the Great Ormond Street Hospital in London. There were no deaths or complications in this group and all patients had “complete relief of pulmonary incompetence” and a reduction in right ventricular hypertension.19 In a discussion of earlier study results, Dr. Bonhoeffer cautioned that this procedure does not remove the patient’s existing pulmonary valve or conduit, as in surgical valve replacement. As a result, the valve obstruction may not be completely resolved. Also, the valve’s durability is not yet known.21

Other researchers are also studying percutaneous valve replacement, but only studies of these devices in animals have thus far been reported.23-25

Surgical or percutaneous valve repair may be used for some types of valve disorders, for example, in percutaneous mitral valvotomy, a balloon catheter is used to open blocked mitral valves. Percutaneous valvuloplasty for aortic stenosis has shown only short-term effectiveness.

Corazón Technologies, Inc. is developing a percutaneous aortic valve repair (PAVR) system, which combines mechanical agitation and the use of a demineralization lavage to remove valve calcification.26
Evalve, Inc. has completed a phase 1 clinical trial [the Endovascular Valve Edge-to-Edge Repair Study (EVEREST I)] of a catheter-delivered clip system for mitral valve repair in 27 patients with severe mitral regurgitation. The company will soon begin enrolment in EVEREST II, a larger multicentre study that will randomize participants to receive the percutaneous clip device or surgical repair. A similar device is also under development at St. Paul’s Hospital in Vancouver, in collaboration with Edwards Lifesciences (Dr. John Webb: personal communication, 2005 Mar 23).

As in other areas of surgery, heart valve replacement is moving towards the use of smaller surgical incisions (minimally invasive or minimal-access surgery with partial rather than full sternotomy), sometimes with robotic assistance.

Also under investigation are sutureless heart valves and tissue-engineered heart valves, which use a patient’s cells or cells from other sources to grow a replacement valve on a biodegradable matrix.

Cholesterol-lowering drugs (HMG-CoA reductase inhibitors or statins) may also play a role in the management of patients with aortic valve disease by slowing the progression of calcification.

Approximately 100 patients worldwide have undergone percutaneous heart valve replacement. The outcomes for many of these patients have not yet been published. Severely ill patients who are unable to undergo surgery are likely to die from existing comorbidities, regardless of whether they receive percutaneous heart valve replacement.

The factors surrounding percutaneous heart valve replacement are similar to those for other new interventional procedures when compared with standard surgical treatment:

- the lack of convincing evidence for the short-term efficacy of the procedures
- the lack of long-term evidence for the longevity and stability of the devices, adverse effects and patient outcomes
- the amount of training and experience required to perfect the implantation of these devices
- the lack of evidence about the advantages and disadvantages of the techniques, imaging methods, devices, delivery systems and post-procedure antithrombotic regimens used by investigators
- the potential cost implications of devices and systems that have not yet reached the market
- the lack of evidence about whether the shorter procedural time, the shorter patient recovery time and the reduced length of hospital stay, which are typically associated with interventional procedures, will significantly affect patients’ quality of life, hospital costs or surgical waiting lists.
Percutaneous heart valve replacement is in an early phase of development. It is too soon to predict whether it offers a clinical advantage or will become an alternative to surgery. If it does, pressures for earlier percutaneous intervention in patients with valve dysfunction may be expected.

It will be several years before most devices used for percutaneous heart valve replacement obtain marketing approval and before longer term patient outcomes are known. The Society of Thoracic Surgeons (STS), the American Association for Thoracic Surgery (AATS) and the Society for Cardiovascular Angiography and Interventions (SCAI) recently issued a position paper outlining the training and clinical trial requirements necessary for further development of percutaneous heart valve replacement procedures.33

References:


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This summary was prepared by Leigh-Ann Topfer; CCOHTA.

This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

This summary has been externally peer reviewed by Dr. James Brophy, Associate Professor, McGill University, Montreal; Dr. Justin Ezekowitz, Cardiology, University of Alberta, Edmonton; Dr. John Webb,* Director Catheterization, St. Paul’s Hospital, Vancouver*.

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