



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



Australia and New Zealand Horizon Scanning Network

**ANZHSN**

AN INITIATIVE OF THE NATIONAL, STATE AND  
TERRITORY GOVERNMENTS OF AUSTRALIA  
AND THE GOVERNMENT OF NEW ZEALAND

# **Horizon Scanning Technology Prioritising Summary**

## **Mini-cardiopulmonary bypass system**

**May 2008  
(updated June 2009)**



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



**Royal Australasian  
College of Surgeons**

© Commonwealth of Australia 2008

ISBN

Publications Approval Number:

This work is copyright. You may download, display, print and reproduce this material in unaltered form only (retaining this notice) for your personal, non-commercial use or use within your organisation. Apart from any use as permitted under the *Copyright Act 1968*, all other rights are reserved. Requests and inquiries concerning reproduction and rights should be addressed to Commonwealth Copyright Administration, Attorney General's Department, Robert Garran Offices, National Circuit, Canberra ACT 2600 or posted at <http://www.ag.gov.au/cca>

Electronic copies can be obtained from <http://www.horizonscanning.gov.au>

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

**DISCLAIMER:** This report is based on information available at the time of research cannot be expected to cover any developments arising from subsequent improvements health technologies. This report is based on a limited literature search and is not a definitive statement on the safety, effectiveness or cost-effectiveness of the health technology covered.

The Commonwealth does not guarantee the accuracy, currency or completeness of the information in this report. This report is not intended to be used as medical advice and intended to be used to diagnose, treat, cure or prevent any disease, nor should it be used therapeutic purposes or as a substitute for a health professional's advice. The Commonwealth does not accept any liability for any injury, loss or damage incurred by use of or reliance the information.

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 departments in all states and territories, the Australia and New Zealand governments; and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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

# PRIORITISING SUMMARY

---

**REGISTER ID** S000076

**NAME OF TECHNOLOGY** MINI-CARDIOPULMONARY BYPASS SYSTEM

**PURPOSE AND TARGET GROUP** PATIENTS UNDERGOING CARDIAC SURGERY WHICH REQUIRES CARDIOPULMONARY BYPASS

## STAGE OF DEVELOPMENT (IN AUSTRALIA)

- |   |   |
|---|---|
| <input 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 checked="" 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
Finland		✓	
France		✓	
Germany		✓	
Italy		✓	
Japan		✓	
Netherlands		✓	
Singapore		✓	
Switzerland		✓	
United Kingdom		✓	
United States		✓	

## IMPACT SUMMARY

Several manufacturers provide a minimally invasive cardiopulmonary bypass system (mini-CPB) with the aim of reducing the deleterious effects of conventional

cardiopulmonary bypass (CPB). The technology is available in specialist medical centres as an alternative to conventional CPB during cardiac surgery.

## **BACKGROUND**

CPB is a form of extracorporeal circulation that maintains blood and oxygen circulation during surgical procedures in which the heart must be arrested or stopped for a period of time. It provides a stationary, bloodless operating field and the ability to easily expose all of the major coronary arteries. Components of CPB, which are connected by a series of tubes, include a venous cannula to remove oxygen deprived blood from the body into a venous reservoir, an oxygenator to remove carbon dioxide and deliver oxygen, a heat exchanger to control blood temperature, a pump to maintain and control blood flow, suction to remove blood from the operative field, and an arterial cannula to return the oxygenated blood to the body via a cardiotomy reservoir (blood storage area).

The use of CPB is mandatory during many cardiac surgical procedures, including coronary artery bypass grafting (CABG) and aortic and mitral valve procedures. CABG surgery is performed in selected patients with significant narrowing and blockage of the coronary arteries due to the build up of fatty plaque (coronary artery disease). The surgery uses veins from the leg or arteries from another part of the body to re-route blood around narrowed and blocked coronary arteries to maintain sufficient blood flow to the heart muscle (Parment et al 2004). Another procedure which typically uses CPB is valve replacement, which is performed in patients with a leaky or partially blocked valve. During such cardiac surgery, CPB oxygenates and recirculates blood that has been diverted from the heart and lungs to allow the surgeon to operate on a non-beating heart (Shann et al 2006).

Conventional CPB has recognised complications. CPB initiates a systemic inflammatory response largely caused by the blood contact with foreign surfaces with subsequent complement activation, pro-inflammatory cytokine secretion and leukocyte activation (Fromes et al 2002). This inflammatory response can lead to cellular damage and potentially to bleeding disorders, respiratory failure, renal dysfunction, neurocognitive decline, multiple organ failure, and death (Bical et al 2006). The heart itself undergoes a local inflammatory reaction due to the ischemia (restricted blood flow) and reperfusion cycle of CPB, and the systemic inflammatory response may exacerbate any heart muscle damage (Fromes et al 2002).

A number of alternatives to conventional CPB have emerged in an attempt to avoid or reduce the systemic inflammatory response. Off-pump (beating heart) coronary artery bypass grafting (OPCAB) avoids the use of CPB by using snares and special instruments on the beating heart to stabilise the artery being bypassed (Parment et al 2004). However, technical problems with OPCAB can include difficulty suturing the graft due to movement of the heart, blood in the surgical field, haemodynamic instability resulting from manipulation of the heart, and myocardial ischaemia (Kamiya et al 2006). In addition, CPB is still required for many complicated cardiac procedures (Valtonen et al 2007). Modifications have also been made to the CPB procedure to reduce the systemic

inflammatory response, including changes to the materials from which the CPB circuit and oxygenator are composed, refinement of the pump and blood circuit, and alterations in priming volume and anticoagulation management (Ranucci & Isgro 2007).

Recently, several manufacturers have developed small biocompatible extracorporeal circulation systems (mini-CPB systems) aimed at reducing the most hazardous aspects of conventional CPB, such as haemodilution and contact of blood with air and foreign surfaces. In contrast to standard CPB, there is no cardiotomy reservoir in the core circuit of the mini-CPB system. These mini-CPB systems incorporate the following features: a closed circuit, centrifugal pump, hollow-fibre oxygenator, biocompatible surfaces, reduced membrane surface area, separation of the pericardial shed blood suction and reduced priming volume (Ranucci & Isgro 2007; Valtonen et al 2007). The biocompatible treatment of the mini-CPB circuit and oxygenator with heparin, phosphorylcholine, or sulphate-sulphonate is designed to limit thrombin formation, platelet count reduction, and inflammatory reaction. Other important changes from conventional CPB are the introduction of a closed circuit which separates the surgical field suction blood, the reduction of the circuit size to reduce haemodilution, and the reduced fluid volume required for priming the system (Ranucci & Isgro 2007). A limitation to this new technology is that many mini-CPB systems have problems handling air trapped in the lines, and this limits their use mainly to isolated CABG procedures rather than valvular and other complex cardiac surgical operations.

Mini-CPB systems which have been developed and used in trials include the mini-extracorporeal circulation system (MECC) (Jostra AG, Hirrlingen, Germany), the Extra-Corporeal Circulation Optimized system (ECC.O) (Dideco Srl, Modena, Italy), the Synergy™ Mini-Bypass System (Cobe Cardiovascular, Inc., Arvada, CO, USA), the CorX (CardioVenton, Inc., Santa Clara, CA, USA), an early Medtronic device and the later Resting Heart® System (RHS) (Medtronic, Inc., Minneapolis, MN, USA). Some mini-CPB systems, such as the RHS, have an additional safety device to detect and eliminate air entering the circuit (Kamiya et al 2006).

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

In Australia, 1.7% of people surveyed in the 2004-05 National Health Survey reported having manifestations of coronary artery disease, which corresponds to around 334,500 Australians affected. In 2003, there were an estimated 49,800 coronary artery disease events (sum of non-fatal hospitalisations for acute myocardial infarction and the number of coronary heart disease deaths in the population) among 40 to 90 year olds, with a fatality rate of 43% for these events. Coronary artery disease accounted for 164,226 hospitalisations in 2003-04, and was the largest single cause of death in Australia in 2004, accounting for 24,576 deaths (19% of all deaths and 51% of cardiovascular deaths) (AIHW 2006). The 2000-01 health expenditure in Australia for cardiovascular disease in general was \$5.5 billion, amounting to 10.9% of the total allocated health expenditure (AIHW 2005). A substantial number of coronary artery disease sufferers undergo CABG and similar procedures requiring CPB each year. In Australia in 2001-02, there were 16,252 CABG operations, with most of these (approximately 90%) requiring CPB

(AIHW 2004; Personal Correspondence 2008). For each patient undergoing CABG the average expenditure for hospital treatment in 1998-99 was \$17,596 per admission, with a long average length of stay in hospital (11.7 days) contributing to this high cost (AIHW 2002).

## **DIFFUSION**

Trials have been published on the use of mini-CPB in a number of countries, including Finland, France, Germany, Italy, Japan, the Netherlands, Singapore, Switzerland and the United States. The United States Food and Drug Administration (FDA) have provided 510k clearance for a number of mini-CPB systems for use, including the MECC in 2002, the RHS in 2003 and the ECC.O in 2005. The CorX was approved in 2003, but has since been withdrawn from the market probably due to financial reasons (Wippermann et al 2005). The FDA also mentions other approved systems, such as the NovoSci Ready System® (NovoSci, The Woodlands, TX, USA) which was listed in 2004 (FDA 2008). No mini-CPB systems are listed in the Australian Register of Therapeutic Goods (ARTG).

## **COMPARATORS**

### **Different models/manufacturers of mini-CPB:**

- MECC
- ECC.O
- RHS
- Synergy
- CorX (no longer manufactured)
- NovoSci Ready system
- Deltastream® (MEDOS Medizintechnik AG, Stolberg, Germany)
- Capiox® (Terumo Corporation, Tokyo, Japan).

### **Different surgical options:**

- Conventional CPB
- OPCAB.

## **SAFETY AND EFFECTIVENESS ISSUES**

At least nine randomised controlled trials (RCTs) were available for MECC, so the two with the largest patient numbers are discussed in this summary. An RCT by Remadi et al (2006) randomly assigned 400 patients undergoing CABG to either conventional CPB (n = 200) or MECC (n = 200), while the RCT by Mazzei et al (2007) compared an elective CABG procedure (isolated myocardial revascularisation via full median sternotomy) performed using either MECC (n = 150) or OPCAB (n = 150).

There was a limited number of RCTs for the other mini-CPB devices. In the RCT by Valtonen et al (2007), 40 patients undergoing elective coronary surgery (CABG) with

extracorporeal perfusion were randomly assigned to conventional CPB or ECC.O, while an RCT by Perthel et al (2007) randomly assigned 60 patients undergoing CABG to conventional CPB (n = 30) or ECC.O (n = 30). Kamiya et al (2006) randomly assigned 20 patients undergoing isolated CABG to conventional CPB (n = 10) or RHS (n = 10), and Huybreghts et al (2007) randomised 49 patients undergoing elective CABG to conventional CPB (n = 24) or Synergy (n = 25).

## **MECC**

Remadi et al (2006) found that C-reactive protein levels (a measure of inflammatory response) were lower after MECC compared to conventional CPB at 24 hours ( $p < 0.01$ ) and 48 hours ( $p < 0.05$ ). Troponin-T levels (a measure of heart muscle damage) were also lower after MECC compared to conventional CPB in the first 24 hours ( $p < 0.01$ ). The mean decrease in haematocrit during MECC was 2.1%. Although there was a significantly greater decrease in the conventional CPB group, the rate and level of statistical significance was not provided. The intraoperative transfusion rate was 6% in MECC and 25.8% in conventional CPB ( $p < 0.001$ ), whereas the postoperative bleeding rate was not significantly different between the groups. The study found that at six hours post-operation the MECC group had lower blood creatinine ( $p < 0.001$ ) and urea ( $p < 0.01$ ) levels (measures of kidney function), and a smaller decrease in platelet levels ( $p < 0.01$ ) compared to the conventional CPB group. There was no difference in leukocyte levels, and no difference between groups for any outcomes by day five post-operation (Remadi et al 2006).

Operative time and intensive care unit time were not significantly different between the two groups (Remadi et al 2006). There was no significant difference in 30-day mortality (three deaths in MECC (1.5%), five in conventional CPB (2.5%)). The causes of death were intestinal bleed (n = 1), sepsis (n = 1) and brain haemorrhage (n=1) in the MECC group, and low-cardiac output syndrome (n = 3), mesenteric ischaemia (n = 1) and respiratory failure (n = 1) in the conventional CPB group. The MECC group had lower rates of postoperative neurological complications ( $p < 0.02$ ), renal failure ( $p < 0.03$ ) and low cardiac output syndrome ( $p < 0.001$ ) compared to conventional CPB. Five MECC and ten conventional CPB patients needed inotropic drugs (to alter the strength of heart muscle contractions) ( $p < 0.03$ ), and one in conventional CPB needed intra-aortic balloon counter-pulsation to treat low cardiac output. Atrial fibrillation was the most frequent postoperative complication in both MECC (28%) and conventional CPB (34%) (Remadi et al 2006).

The study by Mazzei et al (2007) found no significant difference between MECC and OPCAB in interleukin-6 (IL-6) levels (a marker of systemic inflammation) at six hours post-operation when IL-6 levels were at their peak ( $p = 0.14$ ). In addition, the MECC and OPCAB patients had similar blood concentrations of peak creatine kinase (at 24 hours post-operation,  $p = 0.28$ ) and S-100 protein (at end of surgery,  $p = 0.058$ ), which are markers of heart muscle and brain injury respectively. The level of haemodilution in MECC patients was low, with the mean drop in haematocrit being comparable to that of the OPCAB patients ( $p = 0.12$ ). The study authors contrasted this to conventional CPB

which is associated with a mean decrease in haematocrit of 15% as reported in the literature.

Operative time was slightly longer in the MECC group ( $287 \pm 52$  minutes in MECC versus  $256 \pm 63$  minutes in OPCAB,  $p = 0.027$ ) (Mazzei et al 2007). Six patients required emergency conversion to standard CPB, but the study did not report to which groups these patients belonged. Five MECC and two OPCAB patients required treatment for low cardiac output. There was no statistically significant difference between the two groups with respect to hospital mortality rates (two deaths in MECC (1.4%), three in OPCAB (2%),  $p = 0.99$ ), length of intensive care unit and hospital stay, complication rates or need for allogenic transfusion. Postoperative complications (8 in MECC (5.3%) and 10 in OPCAB patients (6.7%),  $p = 0.80$ ) included renal insufficiency, stroke, shock, sepsis and myocardial infarction. After one year, mortality rates (four deaths in MECC (2.7%), five in OPCAB (3.4%)) and rates of angina recurrence or perfusion defect were not significantly different between groups (Mazzei et al 2007).

### **ECC.O**

When comparing inflammation and heart muscle damage in ECC.O and conventional CPB, Valtonen et al (2007) found that blood levels of troponin-T and creatine kinase-MB did not differ significantly between the two groups. The haemoglobin level was significantly higher during perfusion in the ECC.O group ( $p = 0.0069$ ), while additional heparin doses ( $p = 0.018$ ) and the total fluid balance ( $p = 0.0036$ ) were lower compared to conventional CPB. Operative time, duration of intubation following surgery and length of intensive care unit stay and total hospital stay were not significantly different between the treatment groups. There were two acute myocardial infarcts in the conventional group and none in the ECC.O group, but this difference was not statistically significant (Valtonen et al 2007).

Perthel et al (2007) did not report measures of inflammation and heart muscle damage when comparing ECC.O to conventional CPB. The study found no difference in intra- or postoperative blood  $p\text{CO}_2$ ,  $p\text{O}_2$ , base excess and  $\text{HCO}_3$  concentration between the two patient groups, although intraoperative haemoglobin levels were higher in the ECC.O group 'after cardioplegia' ( $p = 0.05$ ) and at the 'cross-clamp off' stage ( $p < 0.05$ ). There was a significant difference in transfusion frequency, with 27% of ECC.O and 43% of conventional CPB patients receiving homologous blood transfusions ( $p = 0.05$ ). In addition, the transfused volume was lower in ECC.O compared to conventional CPB ( $0.53 \pm \text{SD}0.9$  versus  $1.30 \pm 1.93$  units of blood,  $p < 0.05$ ). Fresh frozen plasma was used in three conventional CPB patients and no ECC.O patients ( $p < 0.001$ ). Postoperative bleeding was lower after ECC.O compared to conventional CPB ( $p < 0.05$ ). There were no deaths in either study group (Perthel et al 2007).

### **RHS**

The study by Kamiya et al (2006), which measured inflammation and heart muscle damage, found that at six hours post-operation, the increase in blood leukocyte count was slightly but not significantly lower in the RHS group compared to the conventional CPB group ( $p = 0.10$ ). Blood C-reactive protein levels at 72 hours post-operation were

significantly lower in the RHS group than the conventional CPB group ( $p = 0.045$ ). However, platelet count and levels of creatinine kinase and creatinine kinase-MB were not significantly different between the two groups. There was also no difference in the number of patients in each group requiring intraoperative blood transfusion (four RHS and five conventional CPB patients), and no difference in operative time, mean intubation time and length of stay in intensive care. One patient in the RHS group died on the fifth postoperative day due to cardiac arrest, and atrial fibrillation occurred in two RHS patients and three conventional CPB patients, with no significant difference between groups ( $p = 0.61$ ). No other complications occurred in either treatment group (Kamiya et al 2006).

### **Synergy**

Huybregts et al (2007) quantified inflammatory response by measuring concentrations of leukocytes, IL-6, C-reactive protein and other organ injury markers. Postoperative C-reactive protein concentrations were similar in both groups. However, Synergy, when compared to conventional CPB, produced lower postoperative IL-6 levels ( $p < 0.05$ ) and leukocyte counts ( $p < 0.01$ ). Postoperative urine thromboxane B<sub>2</sub>, an organ injury marker, was significantly lower in the Synergy group compared to the conventional CPB group ( $p < 0.01$ ), as was postoperative urine N-acetyl-glucosaminidase (a measure of renal injury) ( $p < 0.05$ ) and postoperative urine intestinal fatty acid binding protein (a measure of intestinal injury) ( $p < 0.05$ ). Haematocrit levels measured during CPB were significantly higher in the Synergy group compared to conventional CPB ( $p < 0.01$ ). The Synergy group lost fewer platelets during the operation ( $p < 0.01$ ), required less blood products ( $p < 0.04$ ) and had less postoperative blood loss ( $p = 0.04$ ). There was no significant difference in operative time between the two treatment groups. In terms of complications, postoperative atrial fibrillation occurred in seven patients, with no significant difference between the two groups. Neither patient group experienced postoperative myocardial infarction, cerebrovascular or transitory cerebral ischaemic accident, acute renal injury, gastrointestinal complications or in-hospital death (Huybregts et al 2007).

### **COST IMPACT**

Commercially available integrated mini-CPB systems require specific training, have a prolonged learning curve, require team work and are more expensive than conventional CPB (Ranucci and Isgro 2007). However, as yet, there are no studies comparing the cost-effectiveness of mini-CPB to conventional CPB or OPCAB.

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

Mini-CPB may provide an alternative for patients such as Jehovah's witnesses who refuse blood transfusions on religious grounds as it can preserve more haemoglobin than conventional CPB and reduce the need for transfusion (Vaislic et al 2003).

## **OTHER ISSUES**

No other issues were identified from the retrieved material.

## **SUMMARY OF FINDINGS**

A number of RCTs have been published on the safety and effectiveness of mini-CPB during CABG. The two included MECC studies, which assessed several hundred patients, found that inflammatory response and heart muscle damage as measured by surrogate endpoints were significantly lower in MECC compared to conventional CPB and were no different to OPCAB. One ECC.O study found no difference in inflammatory response and heart muscle damage compared to conventional CPB, while the RHS study found that only some inflammatory markers were lower in RHS compared to conventional CPB. The Synergy study found that inflammatory response and organ damage were significantly lower in Synergy compared to conventional CPB. These different results may indicate variations in performance between different mini-CPB systems, and more studies are required to determine if one type of system is superior to another.

Haemodilution during mini-CPB was comparable to OPCAB and was significantly lower than conventional CPB. Intraoperative and postoperative blood loss, as well as blood transfusion requirements, were also lower when mini-CPB was used instead of conventional CPB. Use of mini-CPB resulted in an operative time that was not significantly different to conventional CPB, but was slightly longer than OPCAB. From the included evidence, mini-CPB appears to be at least as safe as conventional CPB or OBCABG. Although there were differences in surrogate endpoints of inflammatory response and heart muscle damage between mini-CPB and conventional CPB, these generally did not translate into differences in complication rates after surgery, with only one included study reporting lower complication rates for mini-CPB compared to conventional CPB. The cost-effectiveness of this technology is yet to be assessed.

## **HEALTHPACT ACTION**

Based on RCT evidence, mini-CPB appears to present a viable alternative to conventional CPB. The studies showed that mini-CPB can be used safely in patients undergoing CABG, and may produce favourable outcomes such as reduced systemic inflammatory response, organ damage and blood loss. However, the operative time appears to be similar to conventional cardiopulmonary bypass and the cost implications of mini-CPB are not clear (e.g. training). Due to its potential, mini-cardiopulmonary bypass systems will be monitored for further developments.

## **NUMBER OF STUDIES INCLUDED**

Total number of studies:	6
Level II intervention evidence	6

## REFERENCES

- Australian Institute of Health and Welfare (AIHW). Coronary Heart Disease. Last updated 2006. <http://www.aihw.gov.au/cvd/majordiseases/coronary.cfm> [Accessed March 2008].
- Australian Institute of Health and Welfare (AIHW). Disease Expenditure. Last updated 2005. <http://www.aihw.gov.au/bod/expenditure/index.cfm> [Accessed March 2008].
- Australian Institute of Health and Welfare (AIHW). Heart, stroke and vascular diseases- Australian facts 2004. Cardiovascular Disease Series No. 22. AIHW Cat. No. CVD 27. Canberra: AIHW and National Heart Foundation of Australia 2004. <http://www.aihw.gov.au/publications/cvd/hsvd04/hsvd04.pdf> [Accessed April 2008].
- Australian Institute of Health and Welfare (AIHW): Mathur S. Epidemic of coronary heart disease and its treatment in Australia. Cardiovascular Disease Series No. 20. AIHW Cat. No. CVD 21. Canberra: Australian Institute of Health and Welfare 2002. <http://www.aihw.gov.au/publications/cvd/echdta/echdta.pdf> [Accessed April 2008].
- Bical O, Fromes Y, Gaillard D, Fischer M, Ponzio O, Deleuze P, Gerhardt M-F, Trivin F. Comparison of the inflammatory response between miniaturized and standard CPB circuits in aortic valve surgery. *European Journal of Cardio-thoracic Surgery* 2006; 29(5): 699 - 702.
- Food and Drug Administration (FDA). Last updated 2008. <http://www.fda.gov/> [Accessed March 2008].
- Fromes Y, Gaillard D, Ponzio O, Chauffert M, Gerhardt M-F, Deleuze P, Bical O. Reduction of the inflammatory response following coronary bypass grafting with total minimal extracorporeal circulation. *European Journal of Cardio-thoracic Surgery* 2002; 22(4): 527 - 533.
- Huybregts R, Morariu A, Rakhorst G, Spiegelberg S, Romijn H, de Vroege R, van Oeveren W. Attenuated renal and intestinal injury after use of a mini-cardiopulmonary bypass system. *Annals of Thoracic Surgery* 2007; 83(5): 1760 - 1767.
- Kamiya H, Kofidis T, Haverich A, Klima U. Preliminary experience with the mini-extracorporeal circulation system (Medtronic resting heart system). *Interactive Cardiovascular and Thoracic Surgery* 2006; 5(6): 680 - 682.
- Mazzei V, Nasso G, Salamone G, Castorino F, Tommasini A, Anselmi A. Prospective randomized comparison of coronary bypass grafting with minimal extracorporeal circulation system (MECC) versus off-pump coronary surgery. *Circulation* 2007; 116(16): 1761 - 1767.

Parment S, Lynn C, Glass R. Coronary artery bypass grafting. *The Journal of the American Medical Association* 2004; 291(15): 1922.

Perthel M, Klingbeil A, El-Ayoubi L, Gerick M and Laas J. Reduction in blood product usage associated with routine use of mini bypass systems in extracorporeal circulation. *Perfusion* 2007; 22(1): 9 - 14.

Ranucci M, Isgro G. Minimally invasive cardiopulmonary bypass: does it really change the outcome? *Critical Care* 2007; 11(2): R45 [Epub ahead of print].

Remadi J-P, Rakotoarivelo Z, Marticho P, Benamar A. Prospective randomized study comparing coronary artery bypass grafting with the new mini-extracorporeal circulation Jostra System or with a standard cardiopulmonary bypass. *American Heart Journal* 2006; 151(1): 198.e1-198.e7.

Shann K, Likosky D, Murkin J, Baker R, Baribeau Y, DeFoe G, Dickinson T, Gardner T, Grocott H, O'Connor J, Rosinski D, Sellke F, Willcox T. An evidence-based review of the practice of cardiopulmonary bypass in adults: A focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. *The Journal of Thoracic and Cardiovascular Surgery* 2006; 132(2): 283 - 290.

Therapeutic Goods Administration (TGA). Australian Register of Therapeutic Goods (ARTG). Last updated 2008.  
<https://www.tgasime.health.gov.au/SIME/ARTG/ARTGPublicWeb.nsf?OpenDatabase>  
[Accessed March 2008].

Vaislic C, Bical O, Farge C, Gaillard D, Ponzio O, Ollivier Y, Abdelmoumen Y, Robine B, Souffrant G, Bouharaoua T. Totally minimized extracorporeal circulation: An important benefit for coronary artery bypass grafting in Jehovah's witnesses. *The Heart Surgery Forum* 2003; 6(5): 307 - 310.

Valtonen M, Vähäsilta T, Kaila-Keinänen T, Kuttilla K. New mini-extracorporeal circulation system (ECC.O) is a safe technique in coronary surgery. *Scandinavian Cardiovascular Journal* 2007; 41(5): 345 - 350.

Wippermann J, Albe J, Hartrumpf M, Kaluza M, Vollandt R, Bruhin R, Wahlers T. Comparison of minimally invasive closed circuit extracorporeal circulation with conventional cardiopulmonary bypass and with off-pump technique in CABG patients: selected parameters of coagulation and inflammatory system. *European Journal of Cardio-thoracic Surgery* 2005; 28(1): 127-132.

## **SOURCES OF FURTHER INFORMATION**

Additional RCTs using a range of mini-CPB machines:

Abdel-Rahman U, Özaslan F, Risteski P, Martens S, Moritz A, Al Daraghmeah A, Keller H, Wimmer-Greinecker G. Initial experience with a minimized extracorporeal bypass system: Is there a clinical benefit? *The Annals of Thoracic Surgery* 2005; 80(1): 243 - 244.

Fromes Y, Gaillard D, Ponzio O, Chauffert M, Gerhardt M-F, Deleuze P, Bical O. Reduction of the inflammatory response following coronary bypass grafting with total minimal extracorporeal circulation. *European Journal of Cardio-thoracic Surgery* 2002; 22(4): 527 - 533.

Nollert G, Schwabenland I, Maktav D, Kur F, Christ F, Fraunberger P, Reichart B, Vicol C. Miniaturized cardiopulmonary bypass in coronary artery bypass surgery: Marginal impact on inflammation and coagulation but loss of safety margins. *Annals of Thoracic Surgery* 2005; 80(6): 2326 - 2332.

Ohata T, Mitsuno M, Yamamura M, Tanaka H, Kobayashi Y, Ryomoto M, Yoshioka Y, Miyamoto Y. Minimal cardiopulmonary bypass attenuates neutrophil activation and cytokine release in coronary artery bypass grafting. *Journal of Artificial Organs* 2007; 10(2): 92 - 95.

Rex S, Brose S, Metzelder S, de Rossi L, Schroth S, Autschbach R, Rossaint R, Buhre W. Normothermic beating heart surgery with assistance of miniaturized bypass systems: The effects on intraoperative hemodynamics and inflammatory response. *Anesthesia and Analgesia* 2006; 102(2): 352 - 362.

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

Mini\$ AND cardiopulmonary bypass  
Mini\$ AND extracorporeal circulation  
MECC  
ECC.O

# **PRIORITISING SUMMARY (2009 UPDATE)**

---

**NAME OF TECHNOLOGY:** MINI-CARDIOPULMONARY BYPASS SYSTEM

**PURPOSE AND TARGET GROUP:** PATIENTS UNDERGOING CARDIAC SURGERY WHICH REQUIRES CARDIOPULMONARY BYPASS

## **2009 SAFETY AND EFFECTIVENESS ISSUES**

A search of relevant databases, online journals and the internet was conducted in May 2009, following the recommendation in May 2008 that mini-cardiopulmonary bypass systems be monitored for 12 months. One meta-analysis and two new randomised controlled trials were selected for inclusion in this update.

The meta-analysis of randomised trials by Biancari and Rimpilainen (2009) identified randomised controlled trials up to June 2008 which yielded 13 studies for analysis. Overall, the analysis included 562 patients in the mini-CPB group and 599 in the conventional CPB group. The investigators noted that mini-CPB patients were older compared to conventional CPB patients (mean difference: 1.45 years,  $p=0.02$ ) but no significant differences were noted for CPB duration or aortic clamping time between both patient groups. Meta-analysis of the available data showed that cumulative mortality rate and length of stay in the intensive care unit was similar between both study groups. Mini-CPB patients had lower cumulative stroke rates (0.2%) compared to conventional CPB patients (2.0%). After the exclusion of series that did not report any postoperative stroke, the investigators found that this complication was significantly lower in mini-CPB patients (odds ratio: 0.25; 95% confidence interval (CI): 0.06 to 1.00;  $p=0.05$ ). Mini-CPB was also associated with significantly lower postoperative blood loss (mean difference: -96.55; 95% CI: -147.48 to -45.62;  $p=0.0002$ ) and higher platelet counts 6 hours post-surgery (mean difference 23480; 95% CI: 2130 to 44830;  $p=0.03$ ). Nevertheless, the risk of re-sternotomy for bleeding was similar between both patient groups (odds ratio: 1.06; 95% CI: 0.32 to 3.57;  $p=0.92$ ). Unfortunately, the authors noted that analysis of post-operative blood transfusion was not possible due to highly variable data. The postoperative incidence of atrial fibrillation was similar between patient groups (Biancari and Rimpilainen 2009).

When analysing patient outcomes after isolated coronary artery bypass surgery, the results presented demonstrated that the operative mortality of mini-CPB patients was similar to conventional CPB patients. However, a significantly lower risk of stroke was evident in mini-CPB patients (0.2% vs. 2.1%; odds ratio: 0.25; 95% CI: 0.06 to 1.00;  $p=0.05$ ). Mini-CPB patients also experienced a significantly lower amount of post-operative blood loss (mean difference: -92.76; 95% CI: -152.9 to -32.92;  $p=0.002$ ). The length of stay within the intensive care unit did not differ between patient groups (Biancari and Rimpilainen 2009).

The randomised controlled trial conducted by Ohata et al (2008) on CABG patients (mini-CPB [Capiiox]: 34 patients; conventional CPB: 64 patients) noted that mini-CPB patients had lower levels of IL-8 on post-operative day 1 ( $8.3\pm 6.4$  vs.  $19\pm 11$  pg/ml;  $p=0.016$ ) and neutrophil elastase on post-operative days 1 ( $127\pm 52$  vs.  $240\pm 100$   $\mu\text{g/L}$ ;  $p=0.013$ ) and 2 ( $107\pm 17$  vs.  $170\pm 45$   $\mu\text{g/L}$   $p=0.0001$ ). In addition, mini-CPB was associated with lower blood loss during ( $620\pm 595$  vs.  $978\pm 658$  mL;  $p=0.012$ ) and after the operation ( $578\pm 310$  vs.  $1002\pm 651$  mL;  $p=0.0034$ ) as well as a lower haemodilution ratio ( $14\pm 2$  vs.  $25\pm 3\%$ ;  $p<0.0001$ ). These results indicate that mini-CPB is a less invasive alternative to conventional CPB (Ohata et al 2008).

The randomised trial by Mozol et al (2008) investigated the cost-effectiveness of mini-CPB compared to conventional CPB in newborns and infants ( $n=60$ , up to 1 year old) undergoing open heart surgery for various indications (e.g. atrial septal defect, ventricular septal defect, transposition of great arteries). The use of mini-CPB reduced priming volume by 46.6% ( $p=0.000001$ ) and blood contact area by 68.8% ( $p=0.0000001$ ). Post-operative treatment duration within the intensive care units (median: 5.13 vs. 11 days;  $p=0.045$ ) and the cardiac care units (median: 1.26 vs. 9.07 days;  $p=0.002$ ) were significantly lower in mini-CPB patients. Duration of treatment within the cardiac care unit was similar between groups. The overall in-hospital treatment duration was significantly lower for mini-CPB patients (20.8 vs. 25.48 days;  $p=0.038$ ). Mini-CPB also resulted in the use of fewer blood products (median 635 vs. 800mL,  $p=0.0007$ ) but the use of infusion fluids were similar for both groups (Mozol et al 2008).

Cost of treatment with regards to inotropic agents, spasmolytic anaesthetics, sedatives and antibiotics were significantly lower for mini-CPB patients ( $p=0.05$ ;  $p=0.045$ ;  $p=0.05$ , respectively). Laboratory tests and microbiological tests were significantly lower as well ( $p=0.04$ ) for mini-CPB patients. The total cost of imaging examinations and other surgical procedures (pleural drainage, delayed closure of chest, insertion and removal of peritoneal dialysis catheter) were similar between both groups. Fixed and variable treatment costs were significantly lower for mini-CPB patients. Median fixed treatment costs include: intensive care unit (2916.41 vs. 4666.26 PLN [polish zloty];  $p=n.s.$ ), cardiac surgery (5006.84 vs. 5301.36 PLN;  $p=n.s.$ ), and cardiology (1654.4 vs. 11927.7 PLN;  $p=0.001$ ). Median variable treatment costs at each unit include: intensive care unit (2149.94 vs. 45227 PLN;  $p=n.s.$ ), cardiac surgery (3729.04 vs. 7278.39 PLN;  $p=n.s.$ ) and cardiology (602.6 vs. 10147.2 PLN;  $p=0.0005$ ). Total post-operative treatment cost was significantly lower with mini-CPB (17375 vs. 26535.38 Euros;  $p=0.037$ ) (Mozol et al 2008).

## **2009 SUMMARY OF FINDINGS**

The meta-analysis by Biancari and Rimpilainen (2009) showed that mini-CPBs appear to confer some form of neuroprotection and resulted in less blood loss compared to conventional CPB while the randomised trial by Ohata et al (2008) suggests that mini-CPB may be less invasive. However, it is important to note that the randomised trials included in the meta-analysis are highly heterogeneous and a large majority had small patient numbers (<50 mini-CPB patients). These results should therefore be interpreted with caution. Mozol et al (2008) highlights that the use of mini-CPD in newborns and

infants (<1 year old) resulted in significantly improved patient outcomes and was accompanied with a significant reduction in overall cost of treatment.

## **2009 HEALTHPACT ACTION**

The evidence on mini-CPB continues to suggest that mini-CPB is a viable alternative to conventional CPB, although the large variability between studies somewhat limits the conclusiveness of the recent meta-analysis. There is some evidence that mini-CPB reduces the cost of treatment, at least in paediatric patients, however additional research is necessary. Further horizon scanning assessment of this technology is not required at this time.

## **2009 NUMBER OF STUDIES INCLUDED**

Total number of studies	3
Level II intervention evidence	3

## **2009 REFERENCES**

Biancari F, Rimpiläinen R. Meta-analysis of Randomized Trials Comparing the Effectiveness of Miniaturized versus Conventional Cardiopulmonary Bypass in Adult Cardiac Surgery. *Heart* 2009 [Epub ahead of print].

Mozol K, Haponiuk I, Byszewski A, Maruszewski B. Cost-effectiveness of mini-circuit cardiopulmonary bypass in newborns and infants undergoing open heart surgery. *Kardiologia Polska* 2008; 66(9): 925-931.

Ohata T, Mitsuno M, Yamamura M, Tanaka H, Kobayashi Y, Ryomoto M, Yoshioka Y, Tsujiya N, Miyamoto Y. Beneficial effects of mini-cardiopulmonary bypass on hemostasis in coronary artery bypass grafting: analysis of inflammatory response and hemodilution. *ASAIO Journal* 2008; 54(2): 207-209.