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Evaluation of CPB devices relative to their capabilities of reducing the transmission of gaseous microemboli (GME) to a patient during cardiopulmonary bypass

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National foreword

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TECHNICAL REPORT

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Evaluation of CPB devices relative to their capabilities of reducing the transmission of gaseous microemboli (GME) to a patient during cardiopulmonary bypass

Évaluation des dispositifs PCP relative à leurs capacités de réduire la transmission des micro-embolies gazeuses (MEG) à un patient durant un pontage cardiopulmonaire

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CH-1214 Vernier, Geneva, Switzerland
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Foreword

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The committee responsible for this document is ISO/TC 150, *Implants for surgery*, Subcommittee SC 2, *Cardiovascular implants and extracorporeal systems*.

Introduction

Present-generation extracorporeal circuit devices are not designed to generate gas bubbles, as was the case with bubble oxygenators, as a function of their mechanism to achieve gas transfer. Gaseous microemboli (GME), while significantly reduced in current extracorporeal circuits, are still detectable.

The presence of GME in blood is not a normal condition and can trigger potentially adverse conditions as both a foreign surface and as a particle or embolus. Adverse systemic sequelae from GME may include activation of blood cells, immune responses, and blockage of blood vessels.

While attributing a causal relationship between GME and significant adverse clinical sequelae is not clear, laboratory equipment and methodology for testing extracorporeal devices on the bench top and are clinically available for use.

This document will review the current scientific literature on GME detection methodologies and their clinical relevance.

GME testing is currently being performed by companies and research groups. Both users and manufacturers will benefit from the creation of standardized terminology for use in this work.

Development of a consensus position on the clinical implications of GME and the capabilities and limitations of currently utilized monitoring equipment will also serve both users and manufacturers.

The currently available monitoring equipment will have a cost impact on all manufacturers and may burden small enterprises more so than existing larger companies. The equipment cost, however, is less expensive than equipment currently required to evaluate many of the extracorporeal devices such as blood gas analysers, cell counters or spectrometers. Independent investigators with such equipment and expertise are also an option.

Evaluation of CPB devices relative to their capabilities of reducing the transmission of gaseous microemboli (GME) to a patient during cardiopulmonary bypass

1 Scope

This document recommends acceptable methodology for conducting gaseous microemboli (GME) testing and discusses limitations of current test methods. Tests described in this document are limited to those conducted using an *in vitro* circulatory system.

This document is applicable to all devices intended for extracorporeal circulatory support during cardiopulmonary bypass (CPB). It outlines approaches currently used to assess the ability of CPB devices to handle GME.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at http://www.iso.org/obp
- IEC Electropedia: available at http://www.electropedia.org/

3.1
cardiopulmonary bypass
extracorporeal circuit used to support a subject's circulatory and gas exchange requirements when the heart and lungs are temporarily functionally excluded from normal circulation during cardiac surgery

3.2
gaseous microemboli
air bubbles present in circulating blood that are in the range 10 µm to 500 µm diameter

3.3
ultrasonic detector
device based on Doppler phenomenon (pulsed or continuous wave) that emits sound signals from a piezoelectric crystal that are reflected from moving blood

EXAMPLE 1 Transcranial Doppler, transesophageal echocardiography, or clamp-on sensors for extracorporeal tubing with the latter used for bench top *in vitro* testing.

EXAMPLE 2 Ultrasonic detectors are able to discriminate circulating particles from background blood flow, and detected reflections (or signals) can be analysed in real time to produce a display of approximate quantities and sizes during the sampling time frame.

3.4
whole blood
fluid used for bench-top studies involving gaseous microbubbles is anticoagulated whole blood

4 Abbreviated terms

CPB cardiopulmonary bypass

GME gaseous microemboli

5 Recommendations

5.1 General

This document addresses current state-of-the-art bench-top testing and is intended to provide guidance to those performing such tests so that reproducible results may be obtained to compare devices. Use of anticoagulated whole blood is noted to provide more relevant results when performing bench-top GME studies. This clause provides testing recommendations.

5.2 Materials and methods

5.2.1 The bench-top circuit should be described in sufficient detail so that an identical circuit can be assembled for additional testing by other parties.

5.2.2 The description of the circuit should include the following:

— physical components, including:
  — tubing dimensions (material, internal diameter, wall thickness, length);
  — types and dimensions of tubing connectors used;
  — manufacturer and model of detector;
  — number, specific location, and method of attachment of detector sensors in the test circuit;
  — other circuit components such as the device being evaluated;
  — type of pump used to circulate blood;
  — presence of a debubbling chamber (if used);
— conditions of the test, including temperature of test fluid, fluid flow rate, establishment of baseline conditions, site of injection of bubbles;
  — hematocrit (should be specified);
  — isotonic solution (shall be used for dilution);
  — anticoagulant used (should be specified);
— evidence of calibration of the bubble detector;
— method of introduction of bubbles into the test circuit (e.g. continuous injection vs. bolus injection), total volume over time of bubbles introduced and means of introduction (e.g. calibrated pump vs. hand injection);
— gas composition (should be room atmosphere only);
— reservoir level when using a hard shell (should be specified);
— volume of blood and the presence (when a soft bag venous reservoir is being tested) and the position of volume regulation mechanism (should be described).

5.2.3 The duration of the test, sampling schedule, and number of tests should be described.

5.3 Results and verification of test

5.3.1 Bubble counts according to the location of the detector sensors should be quantified in terms of sizes and numbers.

5.3.2 The total volume of gas may be reported based on calculations of sizes and numbers.

5.3.3 Results may be reported in numerical or graphical form.

5.3.4 As noted in 5.2.3 above, the number of tests performed under a given set of conditions must be reported with the results, and if the results represent mean values of several tests, this should be noted.

5.4 Components

Components that may be tested include, but are not limited to, one or a combination of the following:

5.4.1 Combination cardiotomy/venous reservoir

This component consists of a hard shell reservoir with multiple inlet connectors and internal chambers used to process either cardiotomy-suctioned blood or venous blood.

These components may contain gross filters and defoamers for removal of large bubbles and blood debris such as large clots or fat particles.

After processing both types of blood, a settling chamber collects the blood for removal by a pump and transmission through the gas exchange section of the oxygenator.

5.4.2 Standalone cardiotomy reservoir

This component is used for processing either cardiotomy-suctioned blood or vent blood.

After processing, blood typically drains by gravity into a larger reservoir and becomes part of the circulating blood.

Processed blood may be sequestered in the reservoir for additional processing by a cell salvage/wash unit.

5.4.3 Standalone venous reservoir, either hard shell or flexible bag type

These components only collect blood from the CPB venous drainage tubing.

5.4.4 Oxygenator with or without integral arterial filter

This component consists of multiple fine strands of hollow fibres containing flowing gas arranged in a configuration to promote mixing of venous blood near the fibre surfaces for gas exchange to take place.

A heat exchanger for circulation of temperature-controlled water most often is integral to the oxygenator.

An integral arterial filter may or may not be part of the oxygenator.

5.4.5 Standalone arterial filter

This component consists of a fine screen mesh fan-folded to provide sufficient surface area for flows used during CPB with an acceptable pressure drop.

5.4.6 Venous bubble trap

This component consists of a chamber intended to trap and remove air bubbles that may be present in the CPB venous tubing.

5.4.7 Blood pump

Either a roller pump or a centrifugal pump may be used in the test circuit.

When using a roller pump, the specifications (e.g. dimensions of pump, tubing inner diameter and type, and method of setting the occlusion) must be described.

When using a centrifugal pump, the model number must be described.

Annex A
(informative)

Rationale for the recommendations of this document

Ultrasonic bubble detectors are commonly used today, both during clinical perfusion (*in vivo*) and in the laboratory (*in vitro*), for measuring bubble activity. Some current-generation CPB circuits have bubble detectors that can be adjusted to distinguish gross bubbles from GME. Ultrasonic detectors have also been used on the CPB circuit at various locations to assess GME removal or production by specific CPB components (e.g. open vs. closed cardiotomy/venous reservoir, roller vs. centrifugal pump or arterial line filter). Echo imaging systems have also been used in recent years (e.g. transesophageal, transthoracic or transcranial) but they are more commonly used to assess effectiveness of cardiac de-airing manoeuvres when cardiac chambers have been opened during valve surgery and are not the subject of this document.

The quantification of GME in some studies has been difficult to verify and reproduce due to lack of standardized calibration techniques. It has been suggested that using commercially available state-of-the-art ultrasonic detectors are better suited in showing trends of GME production or removal instead of absolute numbers or sizes. The intention of this document is to provide an outline for uniform testing and reporting of GME studies conducted under controlled conditions on the bench top so that comparisons may be made between different CPB circuit components.

Bibliography

[1] Butler B.D., & Kurusz M. Guest Editorial, Gaseous microembolism—sources and controversy. *Med. Instrum.* 1985, **19** p. 52

[2] Butler B.D. Biophysical aspects of gas bubbles in blood. *Med. Instrum*. 1985, **19** pp. 59–62

[3] Kurusz M. Gaseous microemboli: sources, causes and clinical considerations. *Med. Instrum*. 1985, **19** pp. 73–76

[4] Butler B.D., & Kurusz M. Gaseous microemboli: a review. *Perfusion*. 1990, **5** pp. 81–99

[5] Kurusz M., Butler B.D., Katz J., Conti V.R. Air embolism during cardiopulmonary bypass. *Perfusion.* 1995, **10** pp. 361–391

[6] Butler B.D., & Kurusz M. Embolic Events. In: *Cardiopulmonary Bypass*, (Gravlee G.P., Davis R.F., Kurusz M., Utley J.R. eds.). Lippincott Williams & Wilkins, Philadelphia, Second Edition, 2000, pp. 320–41.

[7] Melchior R.W. Evaluation of the Maquet neonatal and pediatric Quadrox I with an integrated arterial line filter during cardiopulmonary bypass. *Perfusion*. 2012, **27** pp. 399–406

[8] Ganushchak Y.M. Can minimized cardiopulmonary bypass systems be safer? *Perfusion*. 2012, **27** pp. 176–182

[9] Zanatta P. The role of asymmetry and the nature of microembolization in cognitive decline after heart valve surgery: a pilot study. *Perfusion*. 2012, **27** pp. 199–206

[10] Lin J. Evaluation of Quadrox-i and Capiox FX neonatal oxygenators with integrated arterial filters in eliminating gaseous microemboli and retaining hemodynamic properties during simulated cardiopulmonary bypass. *Perfusion*. 2012, **27** pp. 235–243

[11] Dogal N.M. Evaluation of three hollow-fiber membrane oxygenators without integrated arterial filters for neonatal cardiopulmonary bypass. *Perfusion*. 2012, **27** pp. 132–140

[12] Horton S.B. Integrated oxygenator FX05. *ASAIO J*. 2011, **57** pp. 522–526

[13] Lou S. Generation, detection and prevention of gaseous microemboli during cardiopulmonary bypass procedure. *Int. J. Artif. Organs*. 2011, **34** pp. 1039–1051

[14] Stehouwer M.C. Clinical evaluation of the air removal characteristics of an oxygenator with integrated arterial filter in a minimized extracorporeal circuit. *Int. J. Artif. Organs*. 2011, **34** pp. 374–382

[15] Chaudhuri K. The effect of carbon dioxide insufflation on cognitive function during cardiac surgery. *J. Card. Surg*. 2011, **26** pp. 189–196

[16] De Somer F.M., & Vetrano M.R. Extracorporeal bubbles: a word of caution. *Interact. Cardiovasc. Thorac. Surg*. 2010, **10** pp. 995–1001

[17] Qiu F. Letter: An in vitro comparison of the ability of commonly used pediatric cardiopulmonary bypass circuits to filter gaseous microemboli. *Perfusion*. 2010, **26** pp. 167–168

[18] Roosenhoff T.P.A. Air removal efficiency of a venous bubble trap in a minimal extracorporeal circuit during coronary artery bypass grafting. *Artif. Organs*. 2010, **34** pp. 1092–1098

[19] Yee S. Evaluation of HL-20 roller pump and Rotaflow centrifugal pump on perfusion quality and gaseous microemboli delivery. *Artif. Organs*. 2010, **34** pp. 937–943

[20] Palanzo D. Air-handling capabilities of blood cardioplegia delivery systems in a simulated pediatric model. *Artif. Organs.* 2010, **34** pp. 950–954

[21] Qiu F. Evaluation of Capiox FX05 oxygenator with an integrated arterial filter on trapping gaseous microemboli and pressure drop with open and closed purge line. *Artif. Organs.* 2010, **34** pp. 1053–1057

[22] Salavitabar A. Evaluation of the Quadrox-I neonatal oxygenator with an integrated arterial filter. *Perfusion.* 2010, **25** pp. 409–415

[23] Guan Y., & Su X. Evaluation of Quadrox-i adult hollow fiber oxygenator with integrated arterial filter. *J. Extra Corpor. Technol*. 2010, **42** pp. 134–138

[24] Melchior R.W. An in vitro comparison of the ability of three commonly used pediatric cardiopulmonary bypass circuits to filter gaseous microemboli. *Perfusion.* 2010, **25** pp. 255–263

[25] Resley J. Commentary on: An in vitro comparison of the ability of three commonly used pediatric cardiopulmonary bypass circuits to filter gaseous microemboli. *Perfusion.* 2010, **25** pp. 265–266

[26] Gerriets T. Protecting the brain from gaseous and solid micro-emboli during coronary artery bypass grafting: a randomized controlled trial. *Eur. Heart J.* 2010, **31** pp. 360–368

[27] Myers G.J., & Voorhees C. Post-arterial filter gaseous microemboli activity of five integral cardiotomy reservoirs during venting: an in vitro study. *J. Extra Corpor. Technol.* 2009, **41** pp. 20–27

[28] Wang S.G. Clinical real-time monitoring of gaseous microemboli in pediatric cardiopulmonary bypass. *Artif. Organs*. 2009, **33** pp. 1026–1030

[29] Guan Y.L. Evaluation of membrane oxygenators and reservoirs in terms of capturing gaseous microemboli and pressure drops. *Artif. Organs*. 2009, **33** pp. 1037–1043

[30] Jirschik M. A clinical comparison of bubble elimination in Quadrox and Polystan oxygenators. *Perfusion.* 2009, **24** pp. 423–427

[31] Fiore G.B. Bubble tracking through computational fluid dynamics in arterial line filters for cardiopulmonary bypass. *ASAIO J.* 2009, **55** pp. 438–444

[32] Nyman J. Does CO_2 flushing of the empty CPB circuit decrease the number of gaseous emboli in the prime? *Perfusion*. 2009, **24** pp. 249–255

[33] Groom R.C. Detection and elimination of microemboli related to cardiopulmonary bypass. *Circ Cardiovasc Qual Outcomes.* 2009, **2** pp. 191–198

[34] Gomez D. Evaluation of air handling in a new generation neonatal oxygenator with integral arterial filter. *Perfusion.* 2009, **24** pp. 107–112

[35] Camboni D. Microbubble activity in miniaturized and in conventional extracorporeal circulation. *ASAIO J.* 2009, **55** pp. 58–62

[36] Nielsen P.F., & Funder J.A. Influence of venous reservoir level on microbubbles in cardiopulmonary bypass. *Perfusion.* 2008, **23** pp. 347–353

[37] Riley J.B. Arterial line filters ranked for gaseous micro-emboli separation performance: an in vitro study. *J. Extra Corpor. Technol*. 2008, **40** pp. 21–26

[38] Win K.N. Microemboli generation, detection and characterization during CPB procedures in neonates, infants, and small children. *ASAIO J.* 2008, **54** pp. 486–490

[39] Miller A. Gaseous microemboli detection in a simulated pediatric CPB circuit using a novel ultrasound system. *ASAIO J*. 2008, **54** pp. 504–508

[40] WANG S.G. The capability of trapping gaseous microemboli of two pediatric arterial filters with pulsatile and nonpulsatile flow in a simulated infant CPB model. *ASAIO J.* 2008, **54** pp. 519–522

[41] WANG S.G. Comparison of two different blood pumps on delivery of gaseous microemboli during pulsatile and nonpulsatile perfusion in a simulated infant CPB model. *ASAIO J.* 2008, **54** pp. 538–541

[42] WANG S.G. Delivery of gaseous microemboli with vacuum-assisted venous drainage during pulsatile and nonpulsatile perfusion in a simulated neonatal cardiopulmonary bypass model. *ASAIO J.* 2008, **54** pp. 416–422

[43] SCHREINER R.S. Microemboli detection and classification by innovative ultrasound technology during simulated neonatal cardiopulmonary bypass at different flow rates, perfusion modes, and perfusate temperatures. *ASAIO J.* 2008, **54** pp. 316–324

[44] LYNCH J.E. Microemboli detection on extracorporeal bypass circuits. *Perfusion*. 2008, **23** pp. 23–32

[45] MYERS G.J. Preventing gaseous microemboli during blood sampling and drug administration: an in vitro investigation. *J. Extra Corpor. Technol*. 2007, **39** pp. 192–198

[46] UNDAR A. Detection and classification of gaseous microemboli during pulsatile and nonpulsatile perfusion in a simulated neonatal CPB model. *ASAIO J*. 2007, **53** pp. 725–729

[47] LYNCH J.E. Gaseous microemboli sizing in extracorporeal circuits using ultrasound backscatter. *Ultrasound Med. Biol*. 2007, **33** pp. 1661–1675

[48] PERTHEL M. Clinical advantages of using mini-bypass systems in terms of blood product use, postoperative bleeding and air entrainment: an in vivo clinical perspective. *Eur. J. Cardiothorac. Surg*. 2007, **31** pp. 1070–1075

[49] WOLF L.G. Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: The effect of an aortic side-biting clamp and two clampless devices. *J. Thorac. Cardiovasc. Surg*. 2007, **133** pp. 485–493

[50] DICKINSON T.A., & RILEY J.B. In vitro evaluation of the air separation ability of four cardiovascular manufacturer extracorporeal circuit designs. *J. Extra Corpor. Technol*. 2006, **38** pp. 206–213

[51] YOSHITANI K. Reduction in air bubble size using perfluorocarbons during cardiopulmonary bypass in the rat. *Anesth. Analg.* 2006, **103** pp. 1089–1093

[52] AZARPAZHOOH M.R. Clinical application of transcranial Doppler monitoring for embolic signals. *J. Clin. Neurosci*. 2006, **13** pp. 799–810

[53] HUYBREGTS R.M.A.J.M. First clinical experience with the air purge control and electrical remote-controlled tubing clamp in mini bypass. *Artif. Organs*. 2006, **30** pp. 721–724

[54] SCHOENBURG M. Reduction of gaseous microembolism during aortic valve replacement using a dynamic bubble trap. *Gen. Physiol. Biophys*. 2006, **25** pp. 207–214

[55] RODRIGUEZ R.A. Residual air in the venous cannula increases cerebral embolization at the onset of cardiopulmonary bypass. *Eur. J. Cardiothorac. Surg*. 2006, **29** pp. 175–180

[56] LIEBOLD A. Effect of closed minimized cardiopulmonary bypass on cerebral tissue oxygenation and microembolization. *J. Thorac. Cardiovasc. Surg*. 2006, **131** pp. 268–276

[57] MOTALLEBZADEH R. Letter: Distinguishing solid from gaseous emboli during cardiac surgery. *J. Thorac. Cardiovasc. Surg.* 2005, **129** p. 1194

[58] ABU-OMAR Y. Reply: Distinguishing solid from gaseous emboli during cardiac surgery. *J. Thorac. Cardiovasc. Surg*. 2005, **129** pp. 1194–1195

[59] Russell D. Methods of detecting potential causes of vascular cognitive impairment after coronary artery bypass grafting. *J. Neurol. Sci.* 2005, **229** (Special issue) pp. 69–73

[60] Perthel M. Comparison of conventional extracorporeal circulation and minimal extracorporeal circulation with respect to microbubbles and microembolic signals. *Perfusion.* 2005, **20** pp. 329–333

[61] Abu-Omar Y. Solid and gaseous cerebral microembolization during off-pump, on-pump, and open cardiac surgery procedures. *J. Thorac. Cardiovasc. Surg*. 2004, **127** pp. 1759–1765

[62] Georgiadis D. Doppler microembolic signals during cardiopulmonary bypass: comparison of two membrane oxygenators. *Neurol. Res*. 2004, **26** pp. 99–102

[63] Kurusz M. Bubbles and bypass: an update. *Perfusion.* 2004, **19** () pp. S49–S55

[64] Beckley P.D., & Shinko P.D. A comparison of gaseous emboli release in five membrane oxygenators. *Perfusion*. 1997, **12** pp. 133–141

[65] Strother A., & Wang S. Handling ability of gaseous microemboli of two pediatric arterial filters in a simulated CPB model. Perfusion. 2013, **28** pp. 244–252

[66] Simons A.P., & Ganushchak Y.M. Hypovolemia in extracorporeal life support can lead to arterial gaseous microemboli. *Artif. Organs*. 2013, **37** pp. 276–282

[67] Kieron C., & McMillan D. Microbubble transmission during cardiotomy infusion of a hardshell venous reservoir with integrated cardiotomy versus a softshell venous reservoir with separated cardiotomy: an in vitro comparison. *J. Extra Corpor. Technol*. 2013, **45** pp. 77–85

[68] Doganci S., & Gunyadin S. Impact of the intensity of microemboli on neurocognitive outcome following cardiopulmonary bypass. *Perfusion.* 2013, **28** pp. 256–262

[69] Stehouwer M.C., & Kelder J.C. In vitro air removal characteristics of two neonatal cardiopulmonary bypass systems: filtration may lead to fractionation of bubbles. *Int. J. Artif. Organs.* 2014, **37** pp. 688–696

[70] Simons A.P., & Lindelauf A.A.M.A. Efficacy and safety of strategies to preserve stable extracorporeal life support flow during simulated hypovolemia. *Perfusion.* 2014, **29** pp. 18–24

[71] Johagen D., Appelblad M., Svenmarker S. Can the oxygenator screen filter reduce gaseous microemboli? *J. Extra Corpor. Technol*. 2014, **46** pp. 60–66

[72] Dhami R., & Wang S. In vitro comparison of the delivery of gaseous microemboli and hemodynamic energy for a diagonal and a roller pump during simulated infantile cardiopulmonary bypass procedures. *Artif. Organs*. 2014, **38** pp. 56–63

[73] Wang S., & Chin B.J. Potential danger of pre-pump clamping on negative pressure-associated gaseous microemboli generation during extracorporeal life support; an in vitro study. *Artif. Organs.* 2015, **40** (1) pp. 89–94

[74] Stanzel R.D.P., & Henderson M. An in vitro evaluation of gaseous microemboli handling by contemporary venous reservoirs and oxygenator systems using EDAC. *Perfusion.* 2015, **31** (1) pp. 38–44

[75] Bassett G.C., & Lin J.W. Evaluating the potential risks of bubble studies during echocardiography. *Perfusion*. 2015, **30** pp. 219–223

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