The Mechanical Efficacy of Bubble Traps located in Cardioplegia Delivery Systems in the Prevention of Microemboli Transfer

by
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Abstract

One of the largest postoperative complications of cardiopulmonary bypass during cardiac surgery is neurocognitive impairment. Studies have shown that up to 50% to 70% of Coronary Artery Bypass Graft (CABG) patients present with neurocognitive impairment one-week post-procedure. Most of these deficits have been attributed to gaseous microemboli transfer during CPB at times such as cannulation and perfusionist interventions involving drug administration and blood gas sampling. Although microemboli transfer has significantly improved over the years, it still remains the responsibility of the perfusionist to implement techniques to try and minimize the amount of gaseous microemboli transfer to the patient.

In this study, a cardiopulmonary bypass circuit comprised of two different cardioplegia systems was constructed in order to test the mechanical efficacy of microemboli removal in each. For each, a 1 mL bolus of air was introduced to the circuit pre-cardioplegia and microemboli were measured both pre-cardioplegia and post-cardioplegia using the Emboli Detection and Classification (EDAC) quantifier from Luna Innovations. Additionally, each cardioplegia unit was exposed to two different temperature conditions, normothermia and hypothermia, in order to test whether the solubility impacted microemboli transfer through the systems.

The results of this study showed that the Quest MPS® Myocardial Protection System removed a greater number, and volume, of microemboli than did the Avecor Myotherm ($p<0.05$). However, no impact of temperature was detected. The results of this study demonstrate that selection of cardioplegia setup is a crucial step in attempt on the part of the perfusionists to minimize gaseous microemboli transfer to the patient.

Acknowledgments

This experiment would not have been made possible if it weren't for the input and aid of many individuals over the last 18 months. First, I would like to thank Dr. Ronald Gerrits and Dr. Jeffrey LaMack for consulting and reviewing many different drafts of this document. I would also like to thank all of the clinical perfusionists at Aurora St. Luke's Hospital for guiding and contributing to my development of knowledge in the study and practice of cardiovascular perfusion. Specifically, I would like to thank Jonathan Howard for helping the inspiration and development of this experiment. I would also like to thank Mark Scullion, a fellow Perfusion student, for helping me carry out my experimental trials. Furthermore, I would like to thank my husband, Matthew Ruman, as well as my two sons, Lincoln and Wyatt, for giving me the support and motivation I required to finish my graduate program. This project would not have been possible without the assistance of all of these individuals.

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1.0 Introduction

It was once believed that safely operating on the human heart was impossible. In fact, Theodor Billroth, a well-known surgeon, once exclaimed that "to operate on a human heart was folly at best and ignorance at worst" [1]. This, however, did not stop surgeons from attempting to do so. In 1952, Lewis and his colleagues performed a successful atrial septal defect repair on a five-year-old girl using hypothermia and intermittent inflow occlusion [2]. In 1953, the first successful operation using cardiopulmonary bypass was performed by John Gibbon, who used the mechanical assistance to repair an atrial septal defect in a young woman [2]. Although there were a few successes, these successes were accompanied by multiple failures, and it was quickly discovered that air emboli and inadequate myocardial protection were large contributors to these failures.

One of the largest causes of perioperative mortality that arose from the intermittent cross-clamping technique was the inadequate protection of the myocardium. Although total body hypothermia was instituted, it was not sufficient at preventing myocardial ischemia. In the mid 1950s, Sealy, Young, and colleagues developed a solution containing potassium, magnesium, and neostigmine, which they used for elective cardiac arrest alongside hypothermia; however, due to the skepticism that potassium may cause myocardial damage, the use of chemical cardioplegia did not take in the United States until 1973 [1]. In 1978, Dr. Gerald Buckberg published monumental studies emphasizing reduced postischemic myocardial damage after the modification of calcium, pH, potassium, and osmolarity in the cardioplegic solution, along with the addition of glutamate and aspartate as energy substrates for the myocardium [1]. Furthermore,

Buckberg and colleagues emphasized the use of blood as a cardioplegic vehicle, which was an enormous milestone in the development of myocardial protection [2]. Since then, many different solutions of cardioplegia have been developed, and two of the most commonly used today are Del Nido cardioplegia and whole blood microplegia.

Another large contributor of adverse outcomes during or after cardiopulmonary bypass is air embolism. One of the leading causes of post-CPB neurologic dysfunction, air embolism can also be fatal [3, 4]. Since the development of CPB, many measures to reduce and possibly eliminate microemboli transfer to patients have been developed, including filters, bubble traps, and air bubble detectors. This study investigated the mechanical efficacy of the bubble traps located within two different cardioplegia delivery systems, and their ability to eliminate air introduced to the cardiopulmonary bypass circuit.

2.0 Background

2.1 Types of Cardioplegia Solutions

Myocardial protection is a crucial element in cardiac surgery due to the ischemic time imposed upon the myocardium during the cross-clamp period. The method in which myocardial protection is provided is through administration of a cardioplegic solution, which arrests the heart and provides the heart with depleted energy substrates. The most common way this is achieved is through depolarizing cardiomyocytes and preventing subsequent generation of action potentials [5]. The administration of cardioplegia also allows for a bloodless, quiet field for the surgeon to operate in. Two of the most common cardioplegia solutions used today are Del Nido cardioplegia and Microplegia.

Del Nido cardioplegia was developed in the 1990s by a pediatric cardiac surgeon named Pedro Del Nido [6]. It is a crystalloid solution that is mixed with whole blood at a ratio of 4:1, and is typically dosed at 20 mL/kg every 60 to 90 minutes [6]. The administration pressure of Del Nido is typically 100 to 200 mmHg, with a target flow rate of 200 to 300 mL/min antegrade, through the aortic root [6]. The potassium concentration of this solution is greater than 25 mEq/L, and it is administered cold (< 15 degrees Celsius) [6]. The remainder of the solution contains a Plasma-Lyte A base, magnesium sulfate, mannitol, lidocaine and sodium bicarbonate (Table 1) [6].

Table 1. Del Nido Cardioplegia Contents [6].

Del Nido Cardioplegia Contents		
Ingredients	**Volume (mL)**	**Role**
Plasma-Lyte A	1000	Basic Solution (Na 140 mmol/L; K 5 mmol/L; Mg 3 mmol/L; pH 7.4)
Mannitol 20%	16.3	Osmotic Diuretics; Oxygen Free Radical Scavenger
$MgSO_4$ 50%	4	Ca Channel Blocker; Anti-arrhythmic
$NaHCO_3$ 8.4%	13	pH Buffer
KCL 2 mEq/L	13	Myocardial Depolarization
Lidocaine 1%	13	Sodium Channel Blocker; Hyperpolarizing agent; Anti-arrhythmic

Although originally formulated for pediatric surgery, some institutions have opted to use the cardioplegic solution in adult cardiac surgery as well. This cardioplegia allows for a longer arrest time between doses (60 to 90 minutes), permitting fewer cardioplegia doses, which may decrease the cross-clamp time; however, the large crystalloid volume may lead to increased risk of myocardial edema [6]. Currently, there are no published prospective, randomized trials using Del Nido cardioplegia on adult cardiac patients, but rather only retrospective or propensity matched studies, which limits their true value.

Whole blood microplegia cardioplegia is a modified cardioplegia that consists of blood from the CPB circuit mixed with concentrated additives, as well as an arrest agent-commonly potassium. The possible additives in microplegia may be added to decrease ischemia in the myocardium and include, but are not limited to, magnesium, adenosine, glutamate and aspartate [5]. This type of cardioplegia is usually delivered antegrade and then subsequently retrograde, through the aortic root and coronary sinus, respectively. It is typically delivered cold; however, some opt to start administration with a warm induction dose and administer a “hot shot” of the substrates right before coming off

cross-clamp to replenish the heart of depleted stores. Using this technique, there is less crystalloid volume transferred to the patient, which may be beneficial by decreasing the risk of myocardial edema and hemodilution [7, 8]. Additionally, the higher red blood cell content allows for greater oxygen delivery and better buffering capacity [9]. Microplegia is generally accepted to have the benefits previously noted, but there is also some concern with it. A study performed by Velez found a greater impairment of endothelial function in comparison to Del Nido cardioplegia, potentially from the greater number of neutrophils present in the whole blood cardioplegia [8, 10].

2.2 Delivery Systems for Cardioplegia Administration

There are a variety of systems that can be used to deliver cardioplegia. They each differ slightly, but ultimately are used to achieve the same goal— cardiac protection and quiescence. However, some suggest that cardioplegia delivery systems from different manufacturers are not equivalent in all aspects. Individually they may be superior in blood usage, air handling capabilities, cost effectiveness and overall safety [8]. The two different cardioplegia delivery systems that were investigated in this study are the Avecor Myotherm and the Quest Medical MPS® myocardial protection system.

The Quest Medical MPS® myocardial protection system (Figure 1) has the capability of administering 100% crystalloid, 100% blood, or a ratio system of cardioplegia, with an additive/arrest capacity of 50 mL [11]. The system has a flow rate of 10 to 999 ml/min, prime volume of less than 235 mL (including heat exchanger), and a 16 core-heat exchanger with an integral bubble trap reported to capture ≥100 μL size air bubbles [11]. Additionally, the temperature accuracy of the system is ±1°C [11].

Figure 1. Quest Medical MPS® Myocardial Protection System [11].

The Avecor Myotherm system is a roller pump cardioplegia system that contains a stainless-steel heat exchanger housed within a polycarbonate assembly, which is connected to a second chamber that acts as a bubble trap and air eliminator [12]. The inlet of this chamber is comprised of a hydrophobic membrane, a one-way valve and 150-micron filter screen, intended for air elimination of the cardioplegia prior to passing through the outlet of the chamber (Figure 2) [12, 13]. The Myotherm is intended for a 4:1

cardioplegia to blood ratio; however, it is capable of administering 100% blood cardioplegia, as well [12]. The system has a recommended flow rate of up to 500 mL/min and contains two water ports for attachment of an external heater/cooler [12].

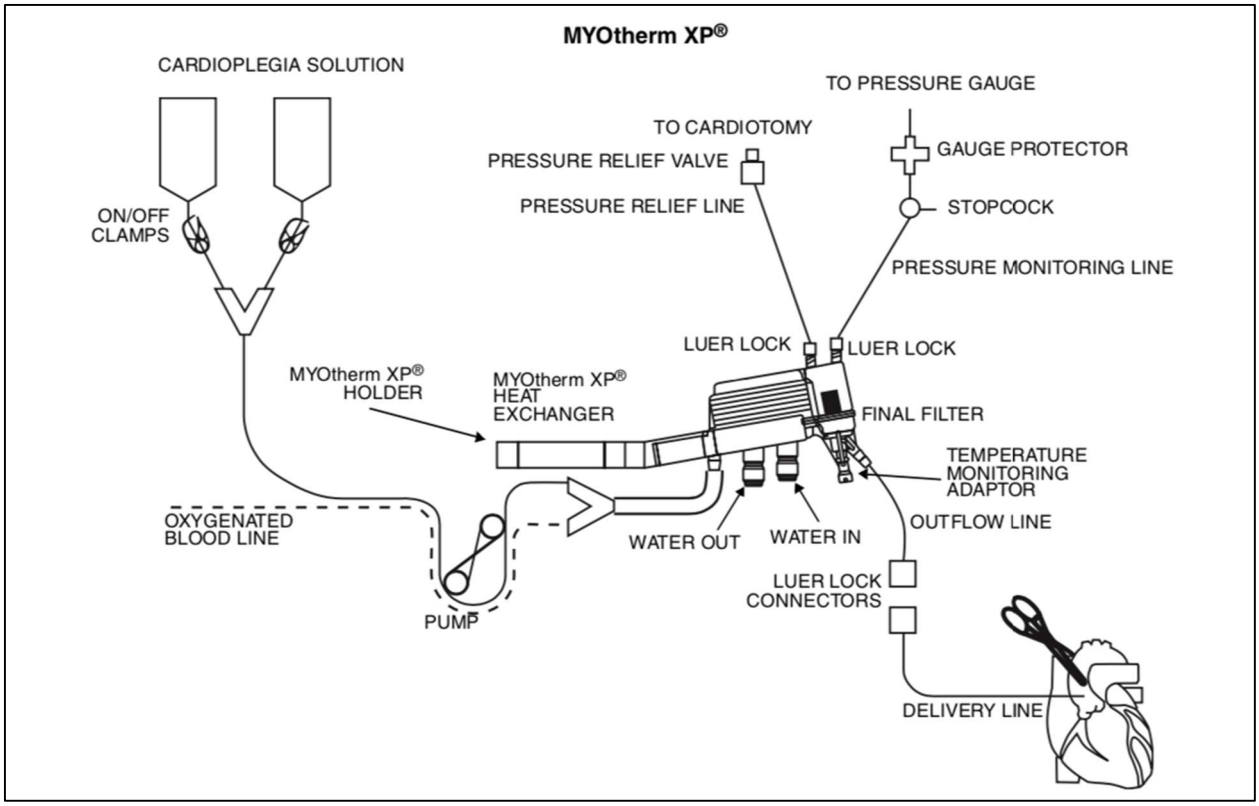

Figure 2. Avecor Myotherm Cardioplegia System [12].

2.3 Sequelae Associated with Microemboli

Although challenging to quantify postoperatively, neurological dysfunction is still considered to be one of the most concerning complications of cardiac surgery involving cardiopulmonary bypass. Studies have reported that 50% to 70% of post-CPB patients

exhibit cognitive deficits one week after CABG procedures and 30% to 40% suffer these deficits long term [14, 15]. Postoperative cognitive decline is believed to be associated with emboli transfer to the cerebral circulation that causes diffuse microischemia, but the origin of the emboli is still highly debated [16]. Several studies have shown that cannulation, initiation of CPB, and perfusionist interventions (cardioplegia and drug administration) are some of the highest incidences of air emboli transfer [14, 15, 16, 17]. The possibility of neurologic dysfunction occurs when microemboli enter the arterial circulation, which in the context of this study, would occur if the heart was not properly deaired and the cross-clamp was removed. In a study performed by Stump *et al.*, more than 10% of the emboli that they detected occurred within two minutes after removal of the cross-clamp [18]. Such air can enter the microcirculation and obstruct the flow of oxygenated blood, causing hypoxia, and necrosis [4]. This can result in damage to the blood brain barrier, which ultimately leads to cerebral swelling and an increase in intracranial pressure [4]. In a study conducted by Bierbach *et al.*, they found increased brain water content in all animals that were exposed to a high embolic load during surgery [19]. Additionally, in a study conducted by Stump *et al.*, a negative, correlating relationship between neuropsychological dysfunction and embolic load was found [18].

Besides neurological complication, the emboli can lodge into the coronary microcirculation, especially during the infusion of cardioplegia or surgical manipulation of the heart, causing ischemia and necrosis distal to the blockage and ultimately resulting in myocardial dysfunction. A unique and important characteristic to be aware of is that air within the circulation has an ability to travel retrograde against the normal physiologic direction of blood flow [20]. This is due to the low specific gravity of the gaseous

microemboli, which allows small bubbles to travel retrograde in veins higher than the heart. This can lead to cerebral venous occlusion or infarct, which is why it is important to ensure that the patient is in Trendelenburg position while removing the aortic cross-clamp [20].

Microemboli also damage the endothelial surface layer by adhering to the vessel wall, impairing solute and water transport across the vessel lumen and lowering the anti-adhesive properties of this cell layer [21]. Barak *et al.* [21] have reviewed the processes involved in these changes, which involve both local inflammatory and coagulation responses. Initiation of the injury is carried out by neutrophils aggregating around the microemboli and producing superoxide, hydroxyl radicals and releasing proteolytic enzymes, and by the foreign surface of the gaseous microemboli directly activating complement proteins C3a and C5a . These molecules then initiate activity of polymorphonuclear cells, histamine release from mast cells, and a resultant increase in vascular permeability. Cytotoxic substances are also released that cause lipid peroxidation in endothelial cell membranes. Finally, the coagulation cascade is activated by the microemboli gas-blood interface, which induces platelet aggregation and ultimately thrombus generation.

2.4 Effect of Temperature on Microemboli

Another factor that might impact the amount of microemboli in CPB circuits is the temperature that cardioplegia is delivered. The solubility of all gases decreases as temperature increases (Figure 3) [22]. Thus, by decreasing the temperature of the cardioplegic solution, hypothetically, the solubility of the gas in the microemboli should

increase, causing it to absorb into the liquid. As a result, the amount of air emboli transfer to the patient during cold cardioplegia administration should decrease.

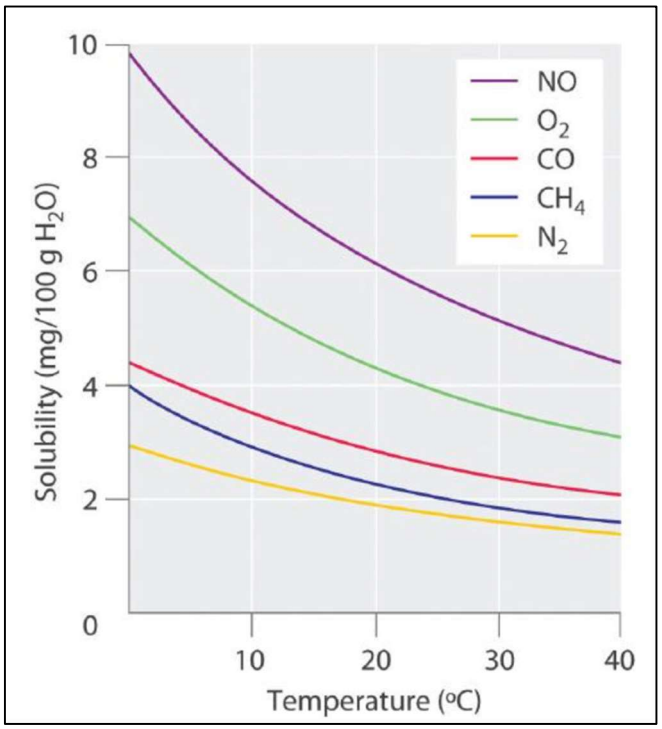

Figure 3. Gas Solubility [22]. Solubility of several common gases in relation to increasing temperature (Celsius) at a partial pressure of 1 atm.

2.5 Hypotheses

Due to the negative effects of gaseous microemboli on the patient's postoperative neurological and myocardial status, gaseous microemboli transfer should be minimized. During cardioplegia administration, the last line of defense against direct air emboli transfer to the patient is the bubble trap located within the cardioplegia unit themselves. In the Quest MPS® system, the heat exchange contains an integral bubble trap that is

reported to capture ≥100 μL size air bubbles, while the Avecor Myotherm contains a 150-micron filter screen to trap air emboli. This study specifically tested the following hypotheses:

- 1: There will be no difference in microemboli volume reduction between the Avecor Myotherm and Quest MPS® cardioplegia systems pre- and post-cardioplegia.
- 2: There will be no difference in microemboli volume reduction between normothermic and hypothermic temperatures pre- and post-cardioplegia.
- 3: There will be no interaction between the different cardioplegia systems and different temperatures on microemboli volume reduction pre- and post-cardioplegia.

3.0 Methods

3.1 Circuit Design

In order to mimic the air handling capabilities of both of the cardioplegia units, a circuit was designed with EDAC microemboli sensors cut in the pre-cardioplegia and post-cardioplegia lines of each cardioplegia administering system. Since this experiment was hypothetical, the arterial-venous loop of the circuit was kept intact, essentially bypassing the patient. The pump that was utilized was a Sarns 8000 heart lung machine, with a Terumo 4,000 mL capacity venous reservoir and Terumo RX25 oxygenator. A partial clamp was placed on the venous line and on the arterial line to mimic vascular resistance of the patient; however, the vascular resistance was not measured. Additionally, a partial clamp was placed on the post-cardioplegia line, in order to mimic the pressure and resistance of the patient's aortic root while giving antegrade cardioplegia, and this pressure was measured on the Quest MPS® system.

The circuit for testing the Quest MPS® cardioplegia system is shown in Figure 4. The inlet line (pre-cardioplegia) originated off of the arterial line, post oxygenator. The outlet line (post-cardioplegia), which normally goes into the patient's aortic root, was connected back into the top of the reservoir. The circuit for testing the Avecor Myotherm was similar (Figure 5), as the pre- and post-cardioplegia tubing placement was identical; however, the tubing coming from the inlet was placed into a roller pump prior to the cardioplegia unit itself. Additionally, there is a separate inlet tubing (pre-cardioplegia) that is used for a crystalloid ratio system, but since this experiment was mimicking blood cardioplegia, this line was primed, and clamped out.

The Quest MPS® system has a built-in heater/cooler and temperature probe that was utilized to monitor and adjust the desired temperatures. For the normothermic trials, 34 to 37 degrees Celsius was targeted and for the hypothermic trials, 8 to 9 degrees Celsius was targeted.

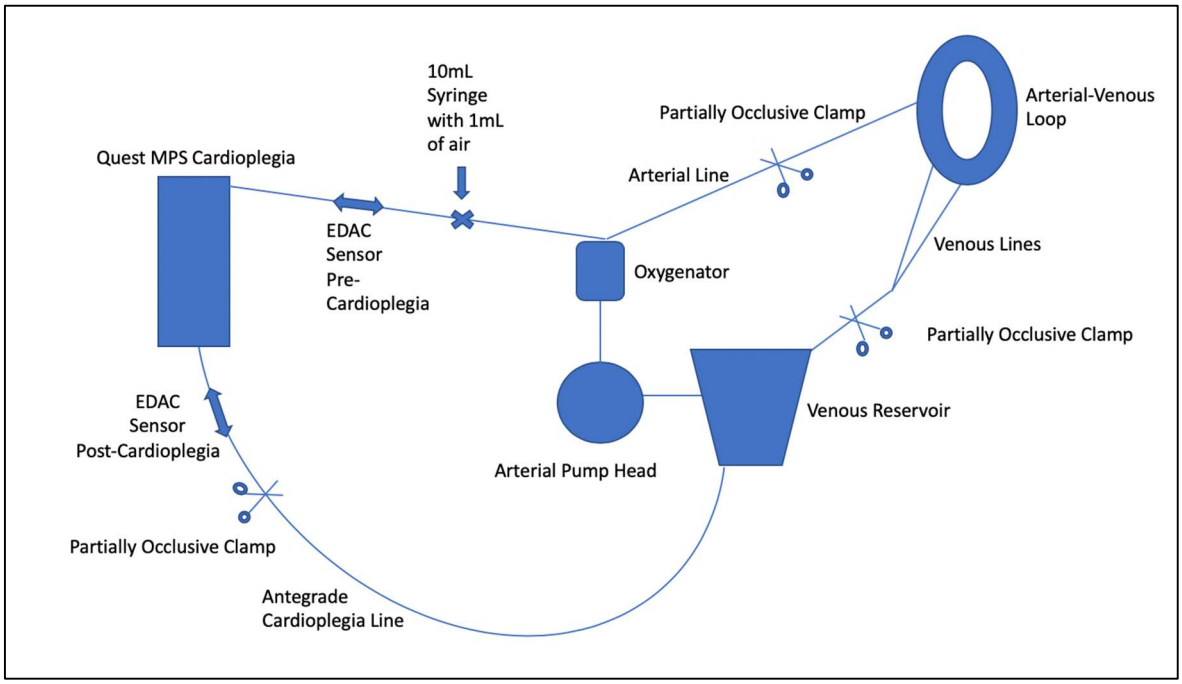

Figure 4. Experimental Circuit with Quest MPS Cardioplegia System.

The Avecor Myotherm does not have an internal heater cooler, so a Medtronic Bio Cal 370 external heater/cooler was connected to the water inlet/outlet ports to achieve the same target temperatures as the Quest trials (Figure 5).

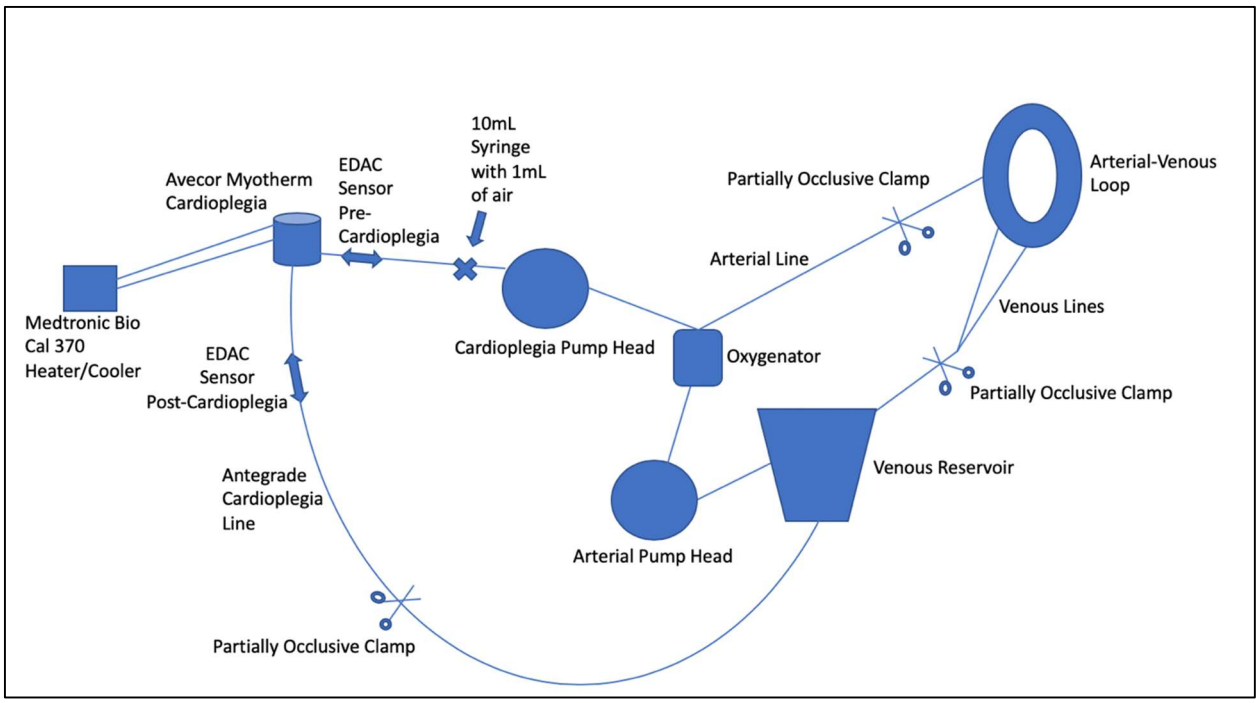

Figure 5. Experimental Circuit with Avecor Myotherm Cardioplegia System and Medtronic Bio Cal 370 Heater/Cooler.

3.2 Emboli Detection

Gaseous microemboli were detected using Luna Innovations Emboli Detection and Classification (EDAC) Quantifier (model 1000). The EDAC quantifier is capable of estimating emboli counts between flow rates of 0.2 and 6.0 L/min, using pulse-echo ultrasound technology [23]. Two EDAC quantifier sensors were placed into the circuit and connected to EDAC transducers using ultrasonic gel, one pre-cardioplegia (Channel 2) and one post-cardioplegia (Channel 1), with simultaneous recording (Figure 6). Data were collected and exported to Microsoft Excel software.

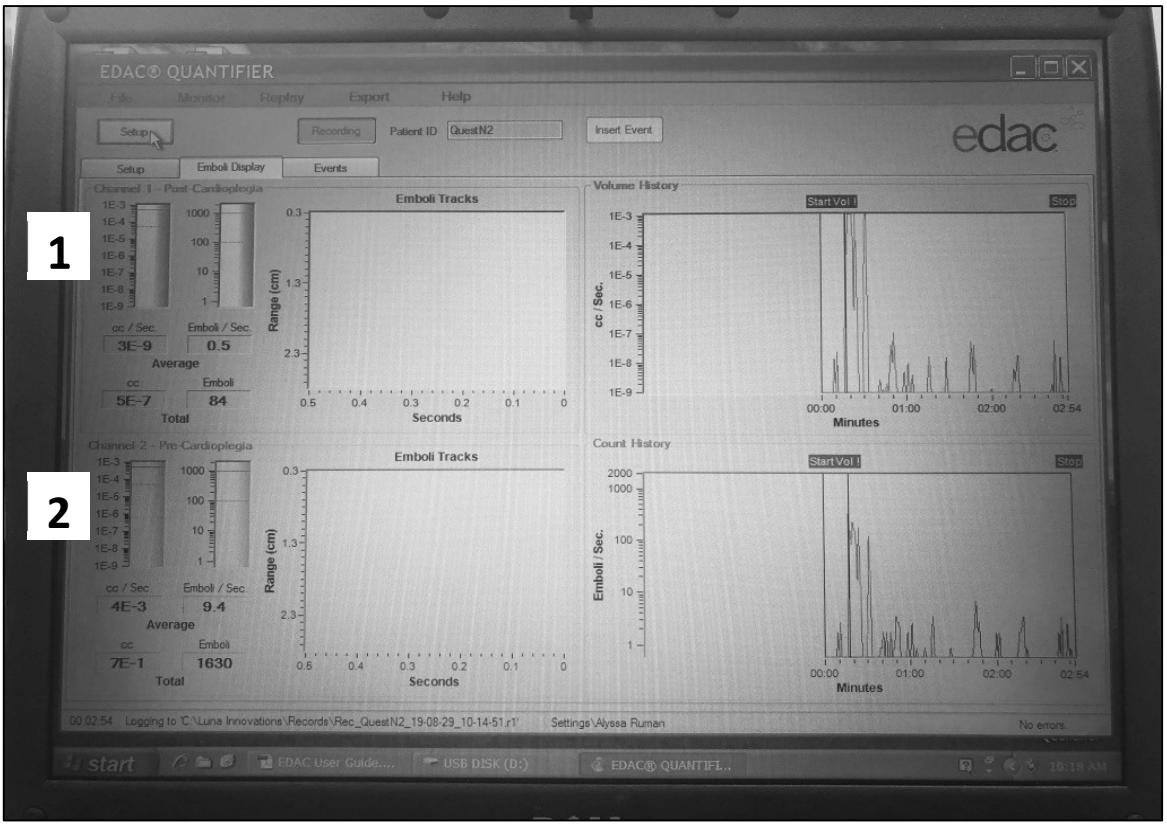

Figure 6. EDAC Quantifier Recording Screen. Visual representation of EDAC Quantifier recording process of both channels. Number 1 represents the post-cardioplegia EDAC sensor, while number 2 represents the pre-cardioplegia EDAC sensor.

3.3 Hypothesis Testing

The circuit was primed with 1600 mL of Plasma-Lyte A solution. The arterial line filter was primed, but then clamped out. The circuit was considered adequately deaired when less than one microemboli per second was detected by the EDAC microemboli sensor. The reservoir level was maintained at 500 mL for all trials.

One liter of antegrade cardioplegia was circulated at a flow rate of 350 mL/min, while the pump head was operating at 4.0 ± 0.5 L/min. Pressure of the antegrade cardioplegia was only measured off of the Quest MPS® unit, since there was a built-in

pressure transducer. The Quest MPS® unit was kept at a pressure range of 130 to 140 mmHg, similar to the infusion pressure into a patient's aortic root. A 1 mL bolus of air was introduced pre-cardioplegia on induction of antegrade administration using a 10 mL syringe connected to a stopcock that was placed into the line proximal to the cardioplegia filters. Five trials were conducted for each of the different variables (combination of cardioplegia system and temperature). Total emboli count and size were measured pre-cardioplegia (post-air bolus) and post-cardioplegia with an EDAC microemboli detector. In between each trial, the circuit was deaired by recirculation and venting (Quest MPS®), and manually deaired (Avecor Myotherm).

Electronic data were recorded in each trial through EDAC channels 1 and 2, post-cardioplegia and pre-cardioplegia, respectively; all data were exported to a Microsoft Excel file. The condensed raw data are summarized in Appendix A.

3.4 Statistical Analysis

The number of emboli recorded for each trial and location were sorted into specific sized bins (0 to 10 microns, 10 to 20 microns, 20 to 30 microns, etc., up to 90 to 100 microns) by the EDAC. Equation (1) was used to calculate the volume of each bin for every individual trial, where n equaled the number of microemboli in each bin, and r equaled the middle radius for each bin. Thus,

$$Volume\ of\ a\ Sphere = n\left(\frac{4}{3}\right)\pi r^3. \quad (1)$$

Next, the volume reduction was calculated by subtracting the pre-cardioplegia volume by the post-cardioplegia volume for each trial, and then converted to milliliters. The data were calculated to represent the percent volume reduction for each trial using

$$Percent\ Volume\ Reduction = \frac{(Pre-cardiople\quad volume)-(Post-cardiop\quad volume)}{Pre-cardioplegi\quad volume} x100. \quad (2)$$

After converting the data, an Anderson-Darling normality test and Levene's equal variance test were conducted on the four data sets corresponding to each cardioplegia-temperature combination.

The data were analyzed using a two-way ANOVA to determine the efficacy of the mechanical bubble traps of the cardioplegia systems at reducing emboli— specifically at normothermic and hypothermic temperatures—and whether there was any interaction between these two independent variables. The dependent variable, percent volume reduction, investigated the difference of emboli volume between pre- and post-cardioplegia, effectively testing the efficacy of the mechanical bubble traps at the two different temperatures. P-values less than 0.05 were considered to be significant.

4.0 Results

An Anderson-Darling normality test was conducted on the four data sets corresponding to each cardioplegia-temperature combination (Table 2). All of the experiment data sets, except for the Avecor Normothermic data set, followed a normal distribution. However, since each of the data sets were balanced, normality is not a strict requirement for performing an ANOVA statistical analysis, which was used for hypothesis testing. A Levene's equal variances test was then performed and indicated the variances were equal (p=0.3885).

Table 2. Normality Tests for Each Set of Trials Associated with Each Variable. *Indicates the only variable whose trials did not follow a normal distribution.

Variable	Anderson-Darling Value	P-Value
Quest Normothermic	0.52	0.0906
Quest Hypothermic	0.41	0.1941
Avecor Normothermic*	0.97	<0.0050
Avecor Hypothermic	0.38	0.2371

Table 3 shows the volume reduction associated with the two different cardioplegia systems and temperatures. These data are also visually represented in Figure 7. The data were then adjusted to follow a normal distribution by calculating the percent volume reduction, shown in Table 4 and visually represented in Figure 8. A significant percent volume reduction was found between the two different cardioplegia systems (p=0.0061), with the Quest MPS® system bubble trap exhibiting a greater reduction in

microemboli total volume than the bubble trap located within the Avecor Myotherm (Figure 10). However, there was no significant difference (p=0.6387) in volume between the different temperatures, and there was no significant interaction between the two independent variables (p=0.4286) (Figure 7).

Table 3. Volume Reduction for Two Different Cardioplegia Systems and Temperatures after 1 mL Air Bolus.

Type of Cardioplegia	Temperature	Volume Reduction (mL) (Mean Volume Reduction ± STD)
Quest MPS®	Normothermic	4.46E-5 ± 1.93E-5
	Hypothermic	2.43E-5 ± 6.29E-6
Avecor Myotherm	Normothermic	1.73E-5 ± 8.04E-6
	Hypothermic	2.02E-6± 1.14E-5

Table 4. Percent Volume Reduction for Two Different Cardioplegia Systems and Temperatures after 1 mL Air Bolus. The Quest MPS® Cardioplegia bubble trap reduced a significantly larger amount of volume than the Avecor Myotherm ($p<0.0001$). There was no significant difference between temperatures in either system, and no significant interaction between temperatures and cardioplegia systems ($p>0.05$).

Type of Cardioplegia	Temperature	Percent Volume Reduction (%) (Mean Percent Volume Reduction ± STD)
Quest MPS®	Normothermic	97.8 ± 1.78
	Hypothermic	91.9 ± 1.64
Avecor Myotherm	Normothermic	79.8 ± 13.6
	Hypothermic	81.3 ± 11.7

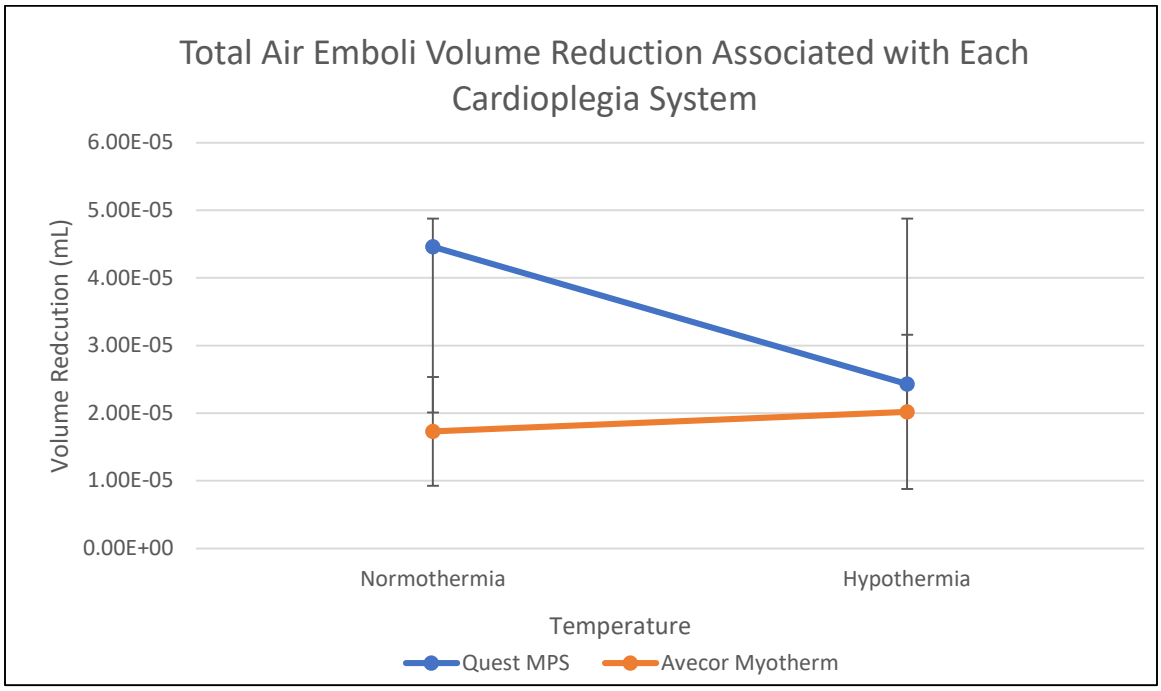

Figure 7. Quest MPS® versus Avecor Myotherm Cardioplegia Systems—Difference in Volume Reduction Pre- Versus Post-Cardioplegia. Error bars represent standard deviation.

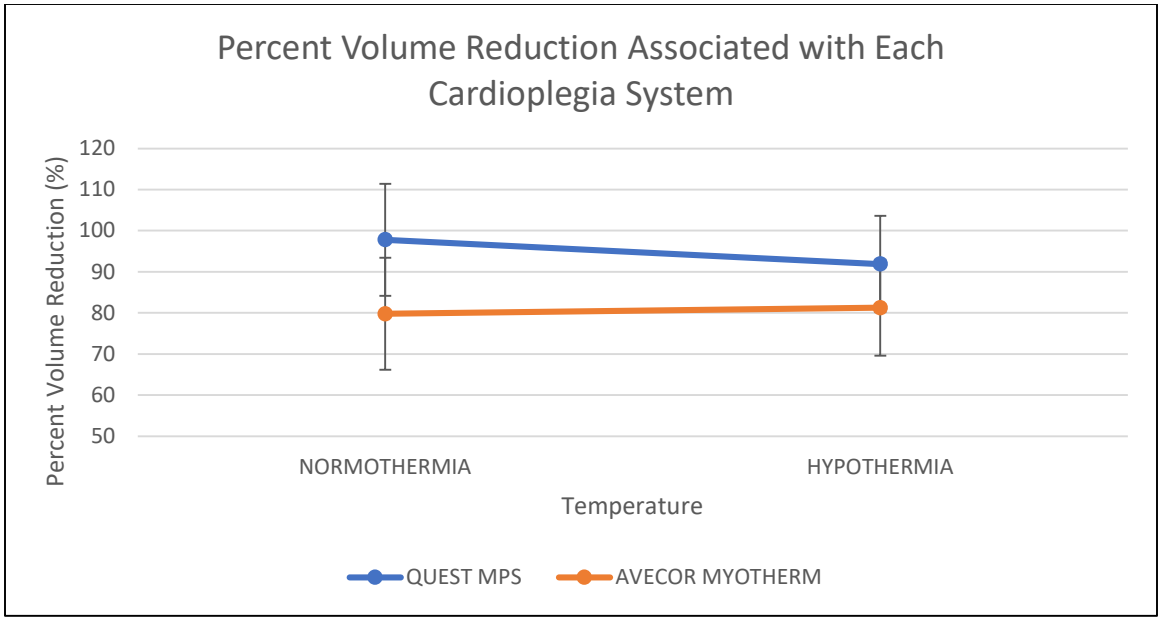

Figure 8. Quest MPS® versus Avecor Myotherm Cardioplegia Systems— Difference in Percent Volume Reduction Pre- Versus Post-Cardioplegia. A significant reduction in percent was only observed between the types of cardioplegia, not the different temperatures. Error bars represent standard deviation.

Figures 9 through 12 represent the percent volume reduction separated into sized bins by microemboli diameter in order to visualize the efficacy of each cardioplegia bubble trap at handing different sized emboli. The figures indicate that both of the cardioplegia system filters are more effective at capturing larger microemboli, compared to small microemboli. However, it is indicated that microemboli diameters in the range 0 to 50 were more effectively reduced by the Quest MPS cardioplegia system than the Avecor Myotherm.

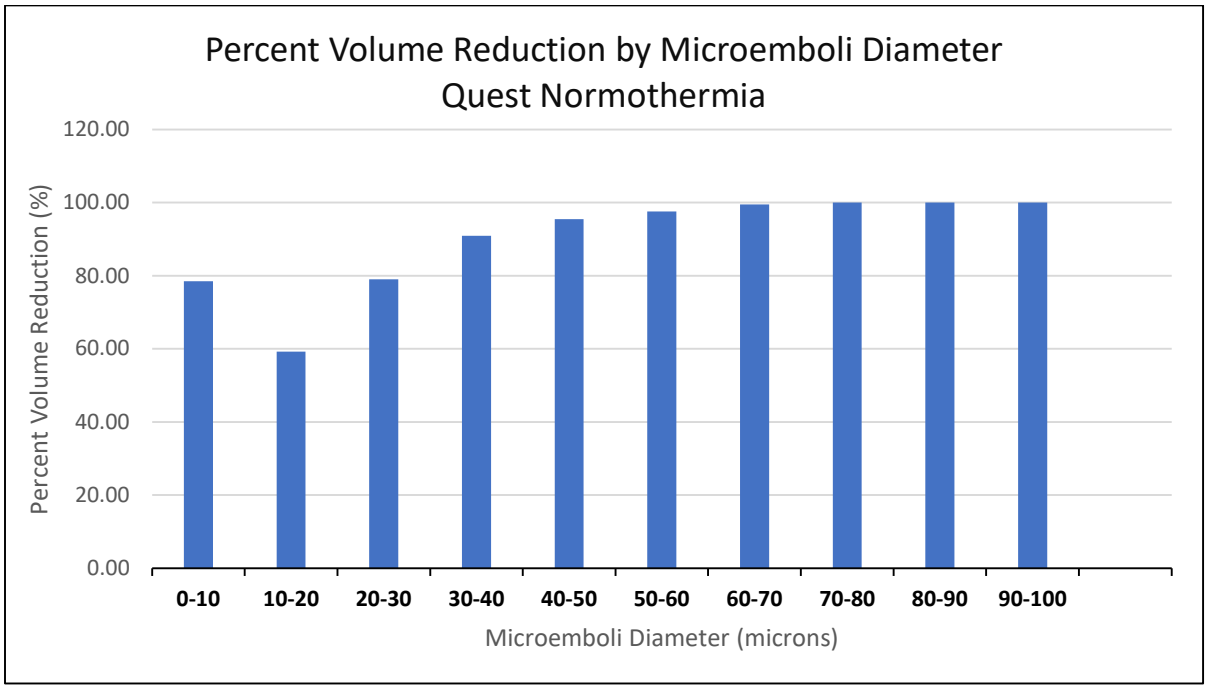

Figure 9. Percent Volume Reduction for Quest Normothermia Trials by Microemboli Diameter (microns). Average percent volume reduction for all Quest MPS normothermia trials.

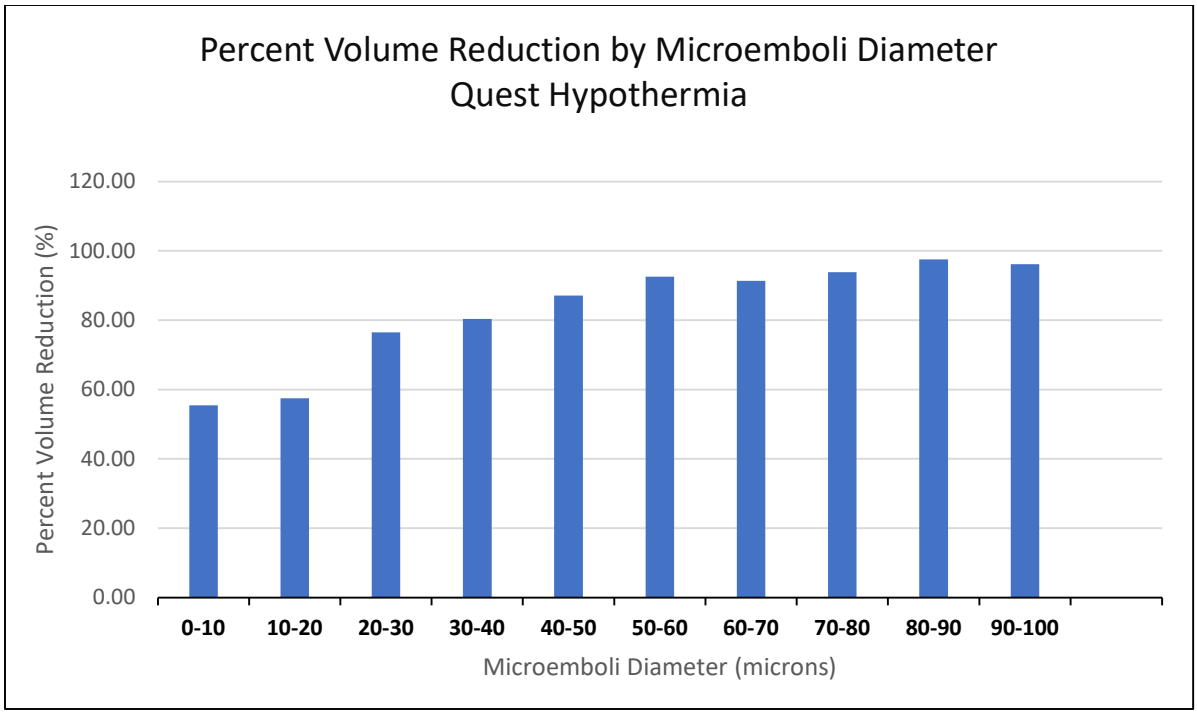

Figure 10. Percent Volume Reduction for Quest Hypothermia Trials by Microemboli Diameter (microns). Average percent volume reduction for all Quest MPS hypothermia trials.

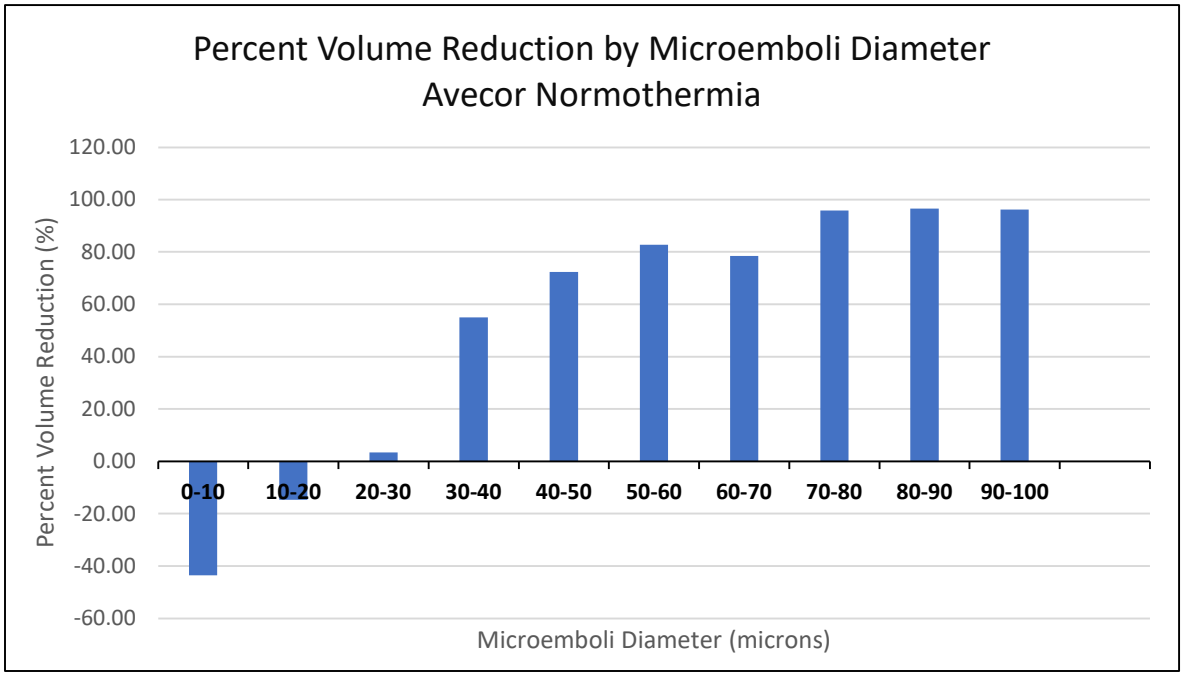

Figure 11. Percent Volume Reduction for Avecor Normothermia Trials by Microemboli Diameter (microns). Average percent volume reduction for all Avecor Myotherm normothermia trials.

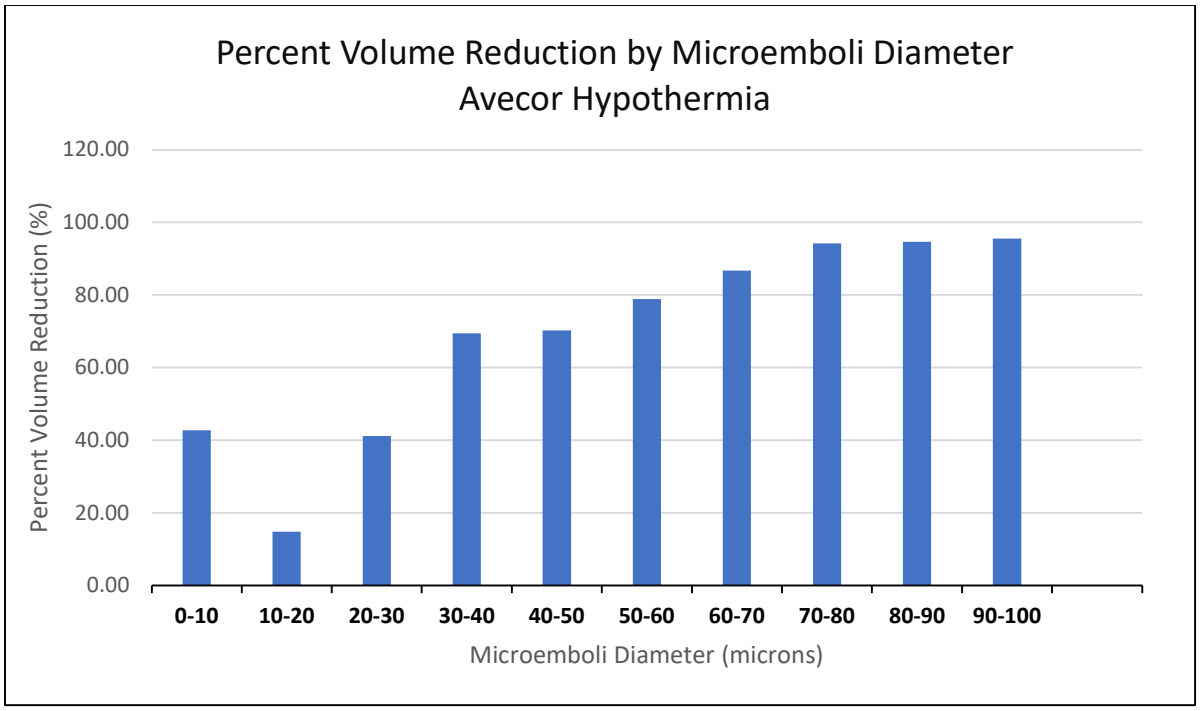

Figure 12. Percent Volume Reduction for Avecor Hypothermia Trials by Microemboli Diameter (microns). Average percent volume reduction for all Avecor Myotherm Hypothermia trials.

5.0 Discussion

This study investigated the mechanical efficacy of the bubble traps located within two different cardioplegia units at normothermic and hypothermic temperatures. It was found that between the two different types of cardioplegia systems, one bubble trap was superior in capturing gaseous microemboli volume. Contrarily, there was no significant difference found between microemboli volume capture between the normothermic versus hypothermic solutions.

The Quest MPS system did a superior job in reducing gaseous microemboli volume. This could be due to the fact that the screen filter captures microemboli greater than 100 microns, whereas the Avecor Myotherm's bubble trap filter is larger, at 150 microns, and therefore unable to catch as many smaller microemboli (<150 microns). This is indicated in the histograms (Figures 9 through 12). Of interest is that Figure 11 shows that the percent reduction is negative for 0 to 30 microns, indicating that more air emboli were detected post-cardioplegia versus pre-cardioplegia. This could indicate that some of the larger emboli that were detected pre-cardioplegia were broken into smaller emboli by the cardioplegia bubble trap. This is significant, as smaller microemboli passed to the patient have been shown to be a source of embolic occlusion in the cerebral microvasculature and can lead to neurological damage post-CPB [21, 24, 25]. Additionally, smaller microemboli can lead to damage of the cerebral endothelium and compromise the integrity of the blood-brain barrier [21, 26]. Therefore, the more effective the filter within the bubble trap, the more likely the emboli transfer to the patient can be minimized.

The cardioplegia was tested at a normothermic temperature (34 to 37 degrees Celsius) and at a hypothermic temperature of (8 to 9 degrees Celsius), and no significant difference was observed in microemboli volume capture. Cold cardioplegia has been a standard practice since the early 1950s due to its ability to lower myocardial oxygen demand and decrease the risk of myocardial damage, whereas the benefits of warm cardioplegia is still a controversial topic [27]. In a meta-analysis conducted by Fan *et al.*, there were no significant difference in all-cause mortality found between the two temperature cardioplegias—however, warm cardioplegia was associated with significantly better post-operative cardiac index, and lower cardiac troponin levels on day 0 [28]. The data from this study do not show that temperature is critical for reducing microemboli transfer through the cardioplegia delivery system.

6.0 Conclusion

6.1 Summary

This study demonstrated that the different filter sizes located within bubble traps inside cardioplegia systems does indeed affect gaseous microemboli volume capture. Based upon the results from this study, it is recommended that the Quest MPS system be implemented in the operating room, rather than the Avecor Myotherm, due to its superior efficacy at eliminating gaseous microemboli.

This study furthers the notion that perfusionists should select their disposables and equipment with respect to evidence-based research in order to minimize the negative effects of gaseous microemboli transfer to patients exposed to cardiopulmonary bypass. Additional precautions that should be employed include the use of available safety devices, adherence to safety protocols, and minimization of perfusionist interventions should also be practiced in order to decrease gaseous microemboli volume transfer.

6.2 Limitations of the Study

Instead of using blood, this study utilized Plasma-Lyte A crystalloid priming solution. The electrolyte composition of Plasma-Lyte A closely mimics that of human plasma with a pH of 7.4, and is therefore considered a “physiological solution” [29]. However, blood additionally contains red blood cells, which were neither included, nor mimicked, in this study and which would impact viscosity of the medium. The viscosity of whole blood at a normal hematocrit is about 3 or 4 times that of water, whereas the viscosity of plasma is only about 1.5 times that of water [30]. Thus, if Plasma-Lyte A’s specifications mimic that of plasma, the viscosity is significantly lower than a patient’s

blood would be (dependent on the patient's hematocrit). This difference in viscosity could significantly vary the dynamic behavior of the gaseous microemboli within the test circuit [31].

Although the Quest MPS® cardioplegia system has a pressure transducer built into the system itself, the Avecor Myotherm cardioplegia system did not. Consequently, while running the cardioplegia units, the pressure was not measured while using the Avecor Myotherm, but was only measured and held consistent while using the Quest MPS® unit. However, the same flow range was used and the post-cardioplegia clamp was not adjusted in between trials in order to provide a consistent resistance and pressure to mimic a patient's aortic root. This pressure was determined using the Quest MPS® cardioplegia unit first prior to starting any trials.

Due to the limited availability of disposables, the experiment could not be randomized or blinded. The circuit required that the trials for each group be conducted successively, with proper deairing techniques in between. Due to the inability to conduct the experiment with randomization, there may have been room for possible biases.

The number of trials for each variable was also limited. This was a very large limitation, and the experiment could have benefited from a larger number of trials to enhance the statistical power. Specifically, it could not be concluded that there was no effect of temperature. This could have been due to an insufficient number of replicates, and would benefit from a larger number of trials.

The method of injecting the air bolus pre-cardioplegia could have been more precise, which would likely eliminate the large differences that were found in the microemboli detected pre-cardioplegia. Although this was adjusted for by calculating the

percent reduction in volume, an ability to compare direct counts could also have been informative. There is also the potential that total volume might impact the ability of the bubble traps to remove maximum volume. This could be tested by injecting varying amounts of volume followed by a determination of the volume reduction. This experiment focused solely on detecting the filtering of microemboli smaller than the advertised filter sizes of the cardioplegia units. This may account for the large discrepancy of volume detected by the EDAC, compared to the 1 mL of injected air.

6.3 Future Research

Although there are noted limitations of this study, this study serves as a more in-depth look at the mechanical efficacy of the bubble traps located in different cardioplegia systems—a topic that is not associated with a significant amount of research. Future studies should consider the use of bovine or donor blood as the fluid medium in order to more adequately mimic a patient's blood viscosity, and therefore, more adequately simulate the dynamic behavior of the bubbles within the vasculature. Another suggestion would be the use of an aortic arch model in order to study the microemboli distribution in the head vessels of a theoretical patient after the removal of the cross-clamp. Finally, testing the ability of the bubble traps to remove air when faced with varying total volumes might be of interest.

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Appendix A: Raw Data

Table A-1. EDAC Channels 1 and 2 Raw Data.

Type of Cardioplegia	Temperature	Trial	Total Emboli Count		
			Pre-Cardioplegia (EDAC Channel 2)	Post-Cardioplegia (EDAC Channel 1)	Difference
Quest MPS®	Normothermic	1	917	253	664
		2	1630	84	1546
		3	1887	88	1799
		4	947	58	889
		5	496	146	350
	Hypothermic	1	1033	182	851
		2	777	184	593
		3	687	193	494
		4	571	158	413
		5	856	164	692
Avecor Myotherm	Normothermic	1	637	241	396
		2	633	503	130
		3	562	302	260
		4	355	184	171
		5	411	237	174
	Hypothermic	1	485	270	215
		2	689	267	422
		3	817	319	498
		4	549	177	372
		5	340	190	150

Table A-2. Calculated Volume Reduction (cubic microns) and Percent Volume Reduction (%).

Type of Cardioplegia	Trials	Volume Reduction	Percent Volume Reduction
Quest	N1	28730755	94.8715573
	N2	61633077	99.17053662
	N3	70553832	99.03931499
	N4	37370465	99.29331318
	N5	19604518	96.51634209
	AVERAGE OF TRIALS	43578530	97.77821284
	H1	29385179	90.34037679
	H2	22284203	93.43244626
	H3	20592451	91.13429095
	H4	15713083	90.42848023
	H5	33283792	94.31857055
	AVERAGE OF TRIALS	24251742	91.93083296
Avecor	N1	25108032	88.52494846
	N2	25859944	85.82089229
	N3	17945588	86.94971735
	N4	13421132	85.09182377
	N5	4132676	52.63101035
	AVERAGE OF TRIALS	17293475	79.80367845
	H1	15129459	79.22219033
	H2	31058269	92.09262549
	H3	35498744	91.40437686
	H4	14665183	83.85213209
	H5	4679041	60.00200827
	AVERAGE OF TRIALS	20206139	81.31466661

Perfusion

Thesis Approval Form

Master of Science in Perfusion – MSP

Milwaukee School of Engineering

This thesis, titled "The Mechanical Efficacy of Bubble Traps located in Cardioplegia Delivery Systems in the Prevention of Microemboli Transfer," submitted by the student Alyssa Ruman, has been approved by the following committee:

Faculty advisor: _____ Date: _____

Dr. Ronald Gerrits

Faculty member: _____ Date: _____

Dr. Jeffrey LaMack

Faculty member: _____ Date: _____

Prof. Jonathan Howard