Abstract - General anesthesia is well known to offer physicians access to a broad variety of invasive procedures otherwise deemed too risky. Anesthesia machines provide the means for anesthetizing patients safely in the hospital operating room. However, these devices are increasingly unable to meet the demands and needs outside of the hospital. Developing countries struggle to purchase and maintain these costly devices, leading to a 40-fold increase in anesthesia-related deaths compared to developed countries. Small-office practices in the United States experience significantly poorer anesthesia outcomes and increased legal claims versus their larger hospital counterparts, resulting in 60% more anesthesia-related deaths. Environmental impacts and global health concerns from the emitted anesthetic gases have brought into serious question the prevailing notion that unchecked emissions were sustainable. These factors can all be attributed to anesthesia machine design and technology having the primary intended use in the traditional operating room. The long-term goal of this work is to develop technologies in anesthesia that expand its safe use, decrease underlying costs, and reduce the total emissions. The immediate objective of this work is to create a feedback-controlled anesthetic gas vaporizer-scavenger system and evaluate its performance. The central hypothesis is that the combined use of mesoporous materials and feedback control provide the opportunity for repeatable capture and release of expired anesthetic gases during anesthesia delivery. Our rationale is that such a device will help reduce the amount of anesthetic needed while simultaneously offering improved control over the delivery of anesthetic gases.

I. INTRODUCTION

Anesthesia is a critical component of most surgical procedures. General anesthetics cause patients to lose consciousness and sensation via suppression of the central nervous systems. Anesthesiologists accomplish this through either intravenous agents or inhalational agents. Delivery of inhalational agents typically necessitates the use of combined ventilator and agent vaporizer, simply known as an anesthesia machine. Anesthesia machines have undergone several major revisions in their design for both practical and safety reasons. The modern anesthesia machine design is a variant of the Boyle anesthesia machine developed in 1917, with the core design today being identical but with the addition of device and patient monitoring and automated safety systems.1-3 These incremental improvements on the anesthesia machine have yielded obvious benefits to the standard operating room. Deliberate addition of safety features combined with integrated patient monitoring has led the field of anesthesia from one of the riskier fields in medicine to one of the safer, with 1 in 1,000 deaths in the 1940s, 1 in 10,000 in the 1970s, and finally 1 in 100,000 by the turn of the century.4–7 However, these improvements are not without their unaddressed problems. Access to proper anesthetic care on a global scale remains shockingly low, with 5 billion individuals having inadequate or no access.8 On a more local basis, the expansion of anesthesia delivered in small-office practices has led to a sudden increase in preventable complications.9-11 Last, the emission of these inhalational agents is becoming an increasing concern as the direct and indirect environmental impact is being better understood and quantified.12-16 Inherently these issues are multi-faceted, however they can in large part be
attributed to the current design of the anesthesia machine. These factors are the basis for identifying and improving a variety of components of the anesthesia machine to ultimately expand the areas of use and reduce the negative impacts imposed by inhalational agent emissions. It is the goal of this dissertation to broaden the body of knowledge related to inhalational agent monitoring, reversible inhalational capture, and design and modelling of these systems.

II. ISSUES IN ANESTHESIA

Alongside the need for patient monitoring, the ability to safely scavenge expired anesthetic gases from the anesthesia machine and away from clinicians remains another hurdle outside of the hospital.\textsuperscript{17,19,20} This hurdle again encourages the use of TIVA over inhalational anesthetics at both increased financial cost and risk of undetected respiratory depression.\textsuperscript{18} Even with appropriate anesthetic scavenging or respiratory monitoring, a secondary impact of inhalational anesthetics is the negative environmental impact.\textsuperscript{13–15} Because the three primary volatile anesthetics (isoflurane, sevoflurane, and desflurane) undergo negligible metabolism in vivo, they are largely exhaled and subsequently scavenged and vented by anesthesia machines to hospital waste gas systems which release these gases to the atmosphere. Studies have estimated that inhaled anesthetic gases contribute upwards of two-thirds of surgical procedure greenhouse gas emissions and 98\% of the ozone depleting compounds.\textsuperscript{16} While not a direct impact to the patient in the operating room, further studies estimate that greenhouse gas emissions associated with US health care activities cause the loss of 123,000-381,000 disability-adjusted life-years annually, well exceeding the 44,000-98,000 who die annual due to preventable medical errors.\textsuperscript{15} In anesthesia, volatile agent release marks the primary environmental burden and are therefore the highest priority for reduction.

1.3 Current Design of Anesthesia Machine

A detailed understanding of the anesthesia machine is needed to identify and address the shortcomings associated with current delivery of anesthesia and will therefore be reviewed. In the most basic sense, the primary role of the anesthesia machine is to deliver fresh oxygen and anesthetic gases to patients during surgery and simultaneously remove exhaled carbon dioxide. This process can be broken down into two sections of the machine: high-pressure and low-pressure (Figure 1). The high-pressure portion of the machine begins with oxygen, air, and nitrous oxide entering the machine from either a hospital supplied pipeline or a gas cylinder. Pressure regulators drop the pressure down to approximately 50 psi. A junction is placed between the nitrous oxide and oxygen lines to fit a fail-safe valve. This valve ensures that nitrous oxide will only flow if there is adequate pressure in the oxygen line, a first step in preventing the accidental delivery of hypoxic mixtures to patients in the event of an oxygen line failure. In tandem with this fail-safe valve, a pressure sensor is often affixed to the oxygen line to additionally alarm in the event of a sudden pressure drop. Moving farther downstream, variable flow control valves allow the clinician to determine the amount of fresh gas entering the vaporizers. Older model anesthesia machines incorporated a coupling chain between the oxygen and nitrous oxide lines to ensure again that a clinician does not erroneously deliver hypoxic mixtures. More modern anesthesia machines accomplish this through computer monitored controls, albeit with limitations and still concern for accidental generation of hypoxic conditions.\textsuperscript{21}

As fresh gas moves into the low-pressure leg of the system, it pass through an anesthetic vaporizer. Modern vaporizers are typically variable-bypass vaporizers. These function by allowing a small amount of fresh gas to by bypassed through a tank filled with the volatile anesthetics. Control over the final concentration is determined by how much fresh gas is bypassed through the tank. Because the vapor pressure of each volatile anesthetic is
different, each vaporizer is carefully calibrated for each specific anesthetic agent. Advanced vaporizers additionally utilize an expansion rod that will further vary the bypass of flow as temperatures change.

This anesthetic rich gas now enters one of three breathing circuit configurations: open, semi-closed/semi-open, or closed. In an open breathing circuit, also known as Mapleson breathing circuit, anesthetic rich gas is delivered to the patient at inspiration, with an adjustable pressure limiting (APL) valve then immediately removing the gas to a waste stream during exhalation. Open breathing circuits are the simplest of breathing circuits, however, fail to reuse any of the exhaled volatile anesthetic gas. Semi-closed/semi-open breathing circuits partially address this by recirculating exhaled volatile anesthetic back into the inspiratory limb. However, this necessitates the addition of a carbon dioxide scrubber to avoid
hypercapnia. These breathing circuits still waste anesthetic rich gas at the same rate is the incoming fresh gas flow. The differentiation between semi-closed and semi-open is based on the fresh gas flows and subsequently the amount of rebreathing. Semi-closed systems have lower fresh gas flow with some rebreathing, while semi-open systems have higher fresh gas flow and little to no rebreathing. Fully closed systems have fresh gas flows that equally match the patient uptake, requiring no addition of a waste stream. This necessitates diligent patient vitals monitoring to match physiologic needs as well as difficulty in accurately titrating the correct inspired anesthetic concentration.

The ventilator that drives the gas coming from the anesthesia machine can exist in a variety of locations in the breathing circuit. Mechanical ventilation methods range from spontaneous respiratory support to complete machine support; however, all ventilators function by increasing the pressure inside the inspiratory limb periodically to facilitate fresh gas entering the lungs. At the junction of the inspiratory and expiratory limb, also known as the Y-piece, gas is sampled to monitor respiratory gases such as oxygen and carbon dioxide as well as anesthetic gases including nitrous oxide and volatile anesthetic agents. Respiratory flow is also monitored at either the Y-piece or through the ventilator to ensure proper ventilation.  

III. Reduction of Anesthetic Gas Emissions

Anthropogenic caused climate change has been receiving a distinct increase in attention from both the public and at research institutions. Carbon dioxide remains the main player in greenhouse gas contribution, representing more than 76% of the total greenhouse gas emissions, primarily from fossil fuel combustion. Fluorinated hydrocarbons, the category of molecules that volatile anesthetic gases fall under, represent a much smaller fraction of greenhouse gas emissions, representing only 2% of the total volume. However, due to the chemical stability of these molecules and subsequent long half-life, most of these gases possess a higher global warming potential compared to carbon dioxide and impose a significant impact on climate change.  

Waste volatile anesthetic gases have little to no economic value and are therefore vented directly into the hospital atmosphere. Consequentially, several technologies have been proposed or developed to remove these compounds, including adsorption, absorption, condensation, membrane separation, or decomposition processing. Of these technologies, adsorption and absorption technologies have seen the most application, in part due to the high operating and capital costs of the other described methods. Despite developments in adsorptive and absorptive methods for capture and regeneration of waste volatile anesthetic gases, the field remains in its infancy. Few publications exist that describe sorption or breakthrough properties of volatile anesthetics with porous media, with most older publications focusing on volatile anesthetics that are no longer used. Other publications review methods for treating waste gases containing volatile organic compounds, however none of these publications are specific to volatile anesthetic emissions and considerations specific to that field. As a result, there exists a broad gap in knowledge for material characterizations describing reversible volatile anesthetic gas capture in both static and dynamic conditions.

1.5.1 Principles of Gas Adsorption

The retention or release of substances onto porous media, especially from a mobile (liquid or gaseous) to a solid phase, is a well-studied field. The curve that describes the retention of the substance onto the porous media at various concentrations is called the “sorption isotherm” and is used to predict the mass transfer of the substance beyond the empirical study. This is described as the solute concentration of the compound compared to the concentration of the
compound on the solid particles, described as P and P0 respectively. Ideally the sorption isotherm would be represented as time-independent capacity, allowing all various reactions to meet equilibrium. However, because many of the intra-molecular retention and release mechanisms are strongly kinetically controlled on time scales beyond practical use, many sorption isotherms will specify time-dependence. The kinetics of these mechanisms can also vary drastically between adsorption and desorption, introducing hysteresis to the sorption isotherm plots.

Based on commonly observed behaviors, sorption isotherms have been described in 6 main shapes by IUPAC. These types of isotherms are characteristic of adsorbents that are microporous (Type I), microporous (Type II, III, and VI), or mesoporous (Types IV and V) are show in Figure 2.28 The hysteresis found in Type IV and V are further classified and are shown in Figure 3. Within these sub-classifications, H1 is reflective of porous materials consisting of cylindrical pore channels or spherical pores. Type H2 is reflective of materials with disordered pore size and shape, especially pore with high tortuosity within the pore. Type H3 and H4 hysteresis both are indicative of slit-shaped pores, with H3 showing no limit to the adsorption at high pressure.

Determining these types of isotherm types is typically done empirically but can provide further insight when used to determine an appropriate model to infer information beyond the collected data. The simplest adsorption isotherm model describes the amount of surface adsorbate as directly proportional to the partial pressure of the gas. The model typically only applies at relatively low concentrations due to the implication that there is no competitive behavior from one adsorbate molecule to another. Thus, the equilibrium of the adsorbate concentrations to the adsorbed phase can simply be described a linear expression also known as Henry’s Law.29

\[
q_e = KP
\]

Where \(q_e\) is the amount of adsorbate at equilibrium, \(K\) is an equilibrium constant, \(P_0\) is the maximum tested pressure, and \(P\) is the pressure of interest.

Langmuir adsorption was derived by Irving Langmuir to describe the gas-solids adsorption as well as to quantify the adsorptive capacities of various adsorbents. The model also assumes monolayer adsorption at the surface of the adsorbate. As a result, this is graphically represented by a Type I isotherm, whereas the sites for adsorption fill, the total surface capacity will be met and no further adsorption can take place, and can be expressed as the following:
Where $Q_0$ is the maximum monolayer coverage capacity, $b$ is the Langmuir isotherm constant, and $C_e$ are the chosen equilibrium concentrations.\textsuperscript{30}

Herbert Freundlich gave provided a basis for modelling reversible adsorption on heterogeneous surfaces that were additionally not restricted to the formation of a monolayer on the surface. This has been found particularly useful for modelling organic compounds on activated carbon and molecular sieves.\textsuperscript{31} The non-linear form of the Freundlich isotherm can be described as:

$$q_e = K_F C_e^{1/n}$$

Where $K_F$ is the Freundlich isotherm constant related to adsorption capacity, and $n$ is the adsorption intensity.

These models provide good insight into the equilibrium capacity pairings of gas-solid phase sorption systems, however as previously mentioned, poses difficulty in accurately described the anticipated kinetics in dynamic systems. When describing the sorption of an adsorbent through a fixed bed of adsorbate, describing and modelling the breakthrough curve is of primary interest. Fast kinetics implies a steep breakthrough curve with rapid adsorption onto the surface of the adsorbate, while slow kinetics will lead to a distended breakthrough curve. Additionally, regardless of any hysteresis in the sorption isotherm, the breakthrough behavior of adsorption versus desorption are widely different in almost all cases.

Modelling of breakthrough curves requires in depth knowledge of the sorption isotherm, particle density and void fraction, kinetics, and fixed-bed dynamics. Experimental data can be used to generate empirical models; however, care should be taken when making predictions as either conditions or materials change. The Wheeler-Robell equation is a simple empirically informed equilibrium model that has had notable success.

The equation-based model applies to any isotherm form and retains simplicity by neglecting the impacts of axial dispersion.\textsuperscript{32}

II. METHODS

Sorption Isotherm of Porous Materials with Anesthetic gases

Two generalized tests were performed to better understand the general behavior of activated charcoal and anesthetic gases. The first test consisted of a 5 L/min flow of oxygen containing 5% isoflurane (Piramal Healthcare Limited, Andhra Pradesh, India) to be passed through a cylindrical vessel containing 42 grams of activated charcoal (Oxpure 1220C-75, Oxbow Activated Carbon, West Palm Beach, FL) until 0.5% isoflurane pushed through (approximately 10 minutes). The vessel was sealed and weighed to determine the amount of anesthetic gas adsorbed onto the surface of the charcoal. Next, a gas flow containing pure oxygen was pushed through the vessel at a rate of 2 L/min and the concentration of anesthetic gas leaving the vessel was measured. The same process was repeated with non-porous beads as a control.

A second test consisted of a smaller vessel containing 10 grams of partially-saturated activated charcoal (total weight of 14 grams) placed between the Y-piece of an anesthesia circuit and a mechanical lung simulator (TTL Michigan Testlung, Michigan Instruments, Grand Rapids, MI). This test lung was then driven using a ventilator and 100% oxygen, with the concentration of isoflurane between the vessel and test lung being monitored. A control was performed with non-porous beads.

Anesthetic Gas Scavenger-Vaporizing Device Test

An initial proof-of-concept prototype was demonstrated and fitted within the rebreathing circuit of a current anesthesia. This system consisted of a housing with two chambers, one fitted with a charcoal cartridge, and the other open to free gas flow. A gear with a semicircular opening was actuated externally to determine which chamber, or combination of chambers, had
fresh gas traveling through from the anesthesia machine to the simulated lung. In addition, differential pressure sensors were attached at both chambers to detect inhalation and exhalation. Anesthetic gas concentration measurements from a standard infrared gas bench was used for basic feedback control. A microcontroller controlled the orientation of the gear valve to titrate the anesthetic concentration based on breath detection, anesthetic gas concentration, and a user input for desired anesthetic concentration using a rudimentary hysteresis controller.

III. RESULTS

A. Sorption Isotherm of Porous Materials
Isoflurane was released at concentrations suitable for anesthesia maintenance for a significant amount of time, approximately 10 minutes (Figure 4). Ventilation was also tested to investigate more dynamic conditions where the device was ventilated with a test lung (Figure 5). Once saturated, the activated charcoal had absorbed approximately 60% of its total weight in isoflurane and was capable of repeatedly reflecting 10% of its total weight in isoflurane or about 3.2 mL of liquid isoflurane. This volume of isoflurane capable of being reflected is the equivalent of anesthesia maintenance at 1 MAC for 1 hour at a fresh gas flow rate of 1 liter per minute.

B. Prototype Device Design
A prototype was successfully created and could perform the basic desired functions. Specifically, inspiratory and expiratory flows were detected and a basic “bang-bang” feedback control was implemented to achieve the desired concentration. Once the charcoal had been saturated from a mock anesthesia induction, the controller was able to maintain average isoflurane concentrations within 0.2% by volume of the user set point (1.2% by volume).

IV. DISCUSSION

Activated carbon has been shown to readily absorb and release anesthetic gases. Creating a system using this material would allow for the implementation of an activated carbon reflector that absorbs, holds, and releases anesthetic gases back to the patient. Not only would this remove the need for an anesthetic scavenging system, but it would also significantly decrease the cost of anesthetic maintenance by reducing the amount of gas vaporized. Preliminary data has shown that 40-mesh activated carbon can capture anesthetic gases and release them with reversed flow at a concentration high enough for sedation. By combining this material with a novel breathing circuit design, we will remove the need for a scavenging system and expand the environments in which anesthesia can be used. Success in this research will ultimately reduce the cost, infrastructure, and expertise needed to deliver general anesthesia. By doing this, the global access to anesthesia and surgical will be greatly increased, reducing the suffering in the world.

Figure 4 The observed concentration of isoflurane leaving the vessel containing 40 grams of saturated activated charcoal as the flow was reversed at 2 liters per minute. The activated charcoal (black) allowed for the gradual released of isoflurane compared to the control (red) containing no activated charcoal.

Figure 5 - The observed concentration of isoflurane during ventilation between 10 grams of activated charcoal and the test lung. Activated charcoal (grey) allowed for the gradual released of isoflurane compared to the control (pink). A running average is shown for both the activated charcoal (black) and control (red).
Future designs will include a dual column system that oscillates between a vaporizing column and a recovering column (Figure 6). The system is designed so that it can be used with the circle breathing system and ventilator of a typical anesthesia machine. In this system one column vaporizes anesthetic gas into the fresh gas flow, while the other column simultaneously scavenges exhaled anesthetic gas from the waste stream. When either the vaporizing column begins to deplete, or the scavenging column begins to fully saturate, a series of valves reverse the roles of each column and continue the process indefinitely. A fresh gas bypass will also be included to both titrate the vaporizing column accordingly and allow for pure oxygen delivery when anesthetic gas is no longer needed. A feedback controller based off an anesthetic gas concentration sensor at the inspiratory limb of the proposed system will further control the fresh gas bypass for increased accuracy and stability. By placing the feedback sensor in the inspiratory limb, the patient remains out of the feedback loop, thereby avoiding regulatory hurdles associated with patient-included feedback control systems like target-controlled infusion. If both columns are depleted and can no longer maintain set anesthetic gas concentrations, a reservoir of anesthetic gas separate from the columns will be used to deliver anesthetic gas and re-saturate the entire system. This system will not require any additional work from the clinician as it will be designed to maintain an anesthetic gas concentration set by the clinician, similar to conventional anesthetic gas vaporizers. However, unlike conventional anesthetic gas vaporizers, this system limits clinicians to a single volatile anesthetic for each case and requires that each column be replaced between cases. While there will still be some remaining volatile anesthetic gas in each discarded column, the overall anesthetic gas used will remain substantially lower.
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