Animal Ventilator for Gated Hyperpolarized Helium MRI

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Abstract

The use of hyperpolarized 3-helium as a contrast agent in functional magnetic resonance imaging (fMRI) is an emerging technique for diagnosing diseases or abnormalities in the respiratory tract. Current methodology allows for fMRI scans to be taken during inhalation of helium every fourth breath. A device and/or method is needed to function as an oxygen ventilator and serve as a means to integrate hyperpolarized helium into the respiratory tract of small animals on every breath. This report outlines three designs that deliver user-defined volumes of gas variable frequencies. Current designs, background, and future work is also discussed.

§1 Problem Statement

Create or redesign a small-animal ventilator capable of delivering constant volumes of hyperpolarized 3-helium and oxygen gas (1-20 mL) at user-specified frequencies (1-100 cycles/min) for safe and compatible use in fMRI.

§2 Intro

Imaging the respiratory tract using traditional MRI methods is very difficult. Our client, Dr. Sean Fain of the Medical Physics Department at the University of Wisconsin – Madison, is using hyperpolarized 3-helium as a contrast agent for fMRI imaging of the respiratory tract. A device is needed to deliver helium and oxygen into a small animal respiratory tract simultaneously, as to allow for imaging of the tract on every breath. This device will help to save our client and other researchers valuable scan time and allow other types of experimental variables to be implemented quickly and easily.

§3 Background

§3.1 Helium MRI

Medical imaging systems are useful in diagnosis and physiological verification. Helium Magnetic Resonance Imaging is a fairly newer technique. It utilizes the same scanner as the conventional MR Imaging, except instead of tuning the scanner to Hydrogen, it is tuned to Helium (48.6 MHz). Therefore, the scanner receives the signal that is coded specifically from Helium.

The Helium is typically inhaled while the MR scanner performs the imaging. The anatomical structures usually imaged with Helium MRI are the respiratory channels and lung systems. During the onset of inhalation, it is possible to see the Helium traveling down the trachea in humans (see Figure 1).

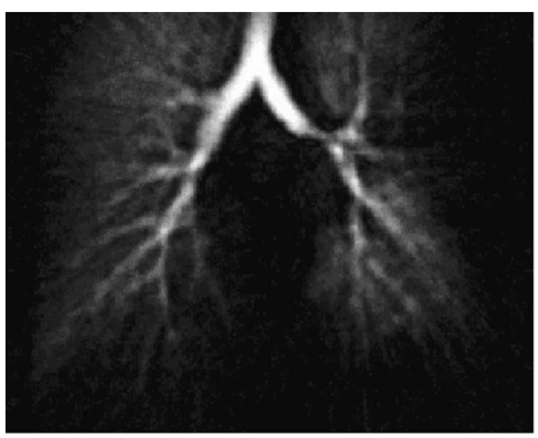

Figure 1. Helium MRI during onset of inhalation. Bright areas indicate regions inhabited by the Helium (1).

The traditional MR scanner receives signal from the hydrogen already in the body. The Helium, however, needs to be hyperpolarized (3-He) in order to be used in this process. The hyperpolarization gives the Helium a heightened spin state. However, oxygen has a paramagnetic effect that destroys the polarization of 3-He. Therefore, great care is taken to avoid mixing the two gases prior to the scanning.

§3.2 Client Study

If 3-He MRI can accurately detect airways and air spaces, one could postulate that respiratory diseases such as asthma could be diagnosed with the use of this process. Ideally, 3-He MRI will successfully reveal information that will lead to diagnoses of respiratory diseases. Doctors will be better able to assess the patient's condition by viewing accurate images of their airway channels and lungs.

This idea is under study by Dr. Sean Fain from the University of Wisconsin Medical School, department of Medical Physics, and his team of researchers. Using an animal model, respiratory diseases are induced to achieve the anatomical effects of a respiratory disease, such as increased airway resistance. Once this is done, 3-He MRI will be performed to confirm the anatomical altercations experienced by the animal from the induced conditions.

The current model administers three breaths of oxygen to the animal and upon the fourth breath of 3-He, the MRI scan is done. The total scan time is currently around 8 minutes per animal. If there was a way to administer 3-He in every breath so that a scan could be performed every breath, the scan time could decrease by a factor of four. However, as stated previously, mixing 3-He with oxygen causes the Helium to lose its polarization. A study was done to quantify the signal loss from mixing oxygen and 3-He and revealed that the total signal loss was less than 5% from that of using a full breath of only 3-He when mixed immediately prior to inhalation (1).

§4 Current Design

The current method of 3-He delivery utilizes two independent systems; the MRI-1 Ventilator, and a modified linear stage-mover device that propels the helium breaths. The entire unit can be visualized in the block diagram shown in Figure 2.

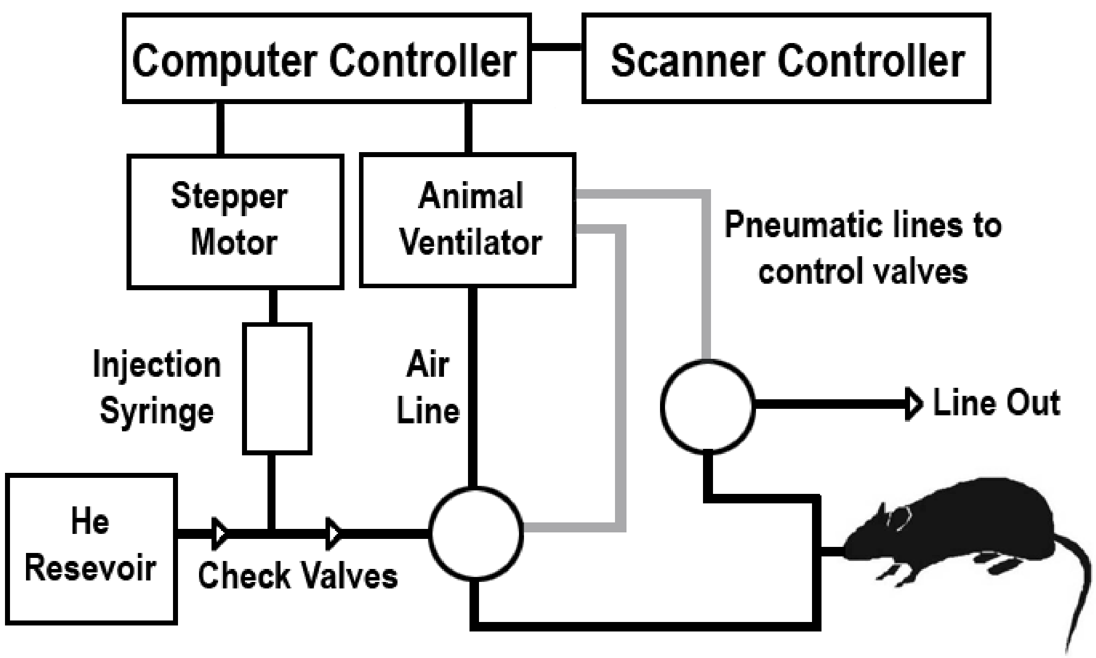

Figure 2. Current setup of gas injection system used by client.

The entire configuration is run from a single computer. This computer controls the MRI scanner and the ventilator setup so that the images can be collected simultaneously as the helium breath is delivered. The ventilator can be controlled either manually or from the computer controller and the stepper motor is controlled by an existing LabView program.

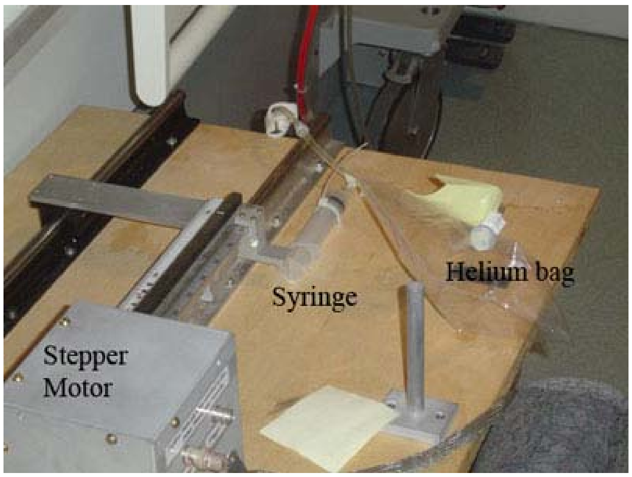

Figure 3. Syringe and 3-He reservoir bag.

Helium is delivered via the pumping of a 10 mL syringe mounted to a 4’x 2’ board. Also on this board is a large stepper motor, controller unit, and linear slide (Figure 3). The stepper motor rotation causes the linear slide to move a specified distance depending on the desired tidal volume to be delivered. The syringe is attached to the linear slide and He gas is delivered to the tubing connected to pneumatic valves that lead to the animal. As the plunger is pulled back into position, gas is moved from a helium holding reservoir, through a one-way check valve, and into the syringe to be stored until the next helium breath needs to be delivered.

The ventilator is used to not only to supply the air to the small animal, but also to serve as a control mechanism for the pneumatic valves (Figure 4). The pneumatic control lines are pressurized at about 40 psi and drawn from the wall outlet. When a breath is to be delivered, the control lines exert a pressure on the pneumatic valves, opening them and (depending on the breath) allow the passive air line or the helium line to enter the tracheal tube for inhalation or allow for passive exhalation from the animal.

The ventilation system now in place works. However, it is very large and does not allow for helium to be delivered on every breath. It is suggested to change the current setup from the previously described system to one that integrates He and O_2 into every breath. The block diagram in Figure 5 shows a suggested redesign of the setup.

Figure 4. Current ventilator with gas lines (red) to run pneumatic valves.

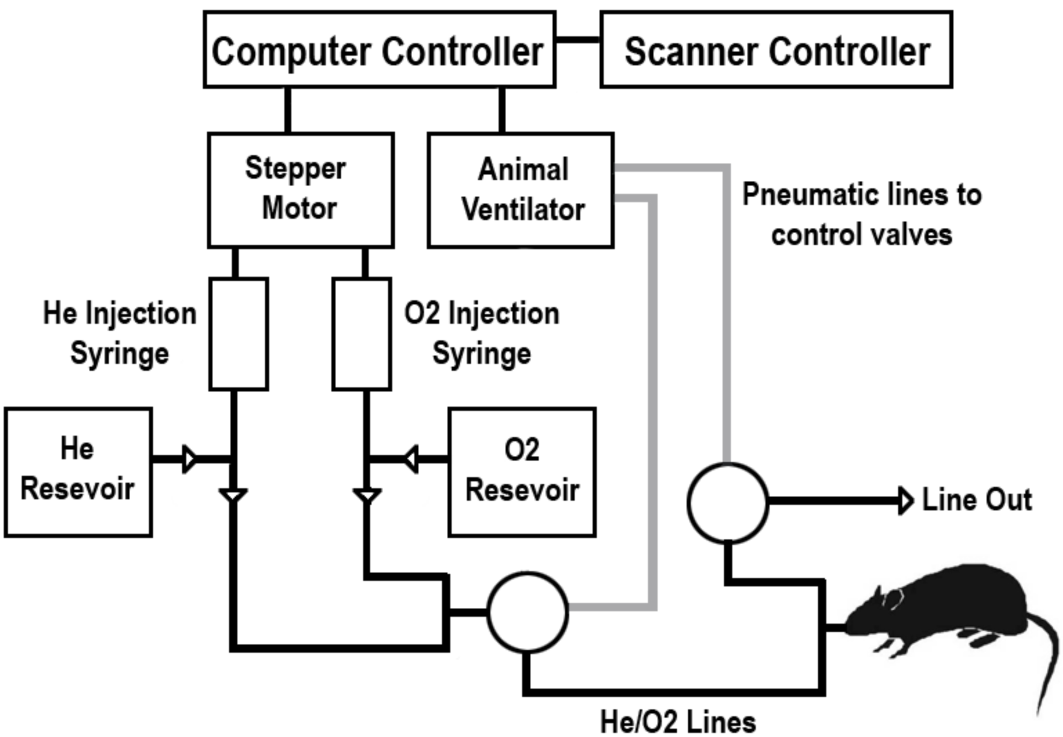

Figure 5. Modified setup desired by client.

In this design, the passive air supply is turned into a driven air source and powered simultaneously with the helium supply. This way, a known ratio of He and O_2 can be delivered on every breath. The ventilator is still used, but in this case only to control the pneumatic inhalation/exhalation valves.

§5 Literature Search

A literature search for ventilators capable of functioning in the way the client desires showed that there are few, if any, ventilators that describe a way of administering the desired mixture of gasses. Ventilators similar to USPTO patent 5,107,830 or the setup described in 5,752,506 might be used as a reference, however by themselves, do not describe an appropriate mechanism. Some patents were found that describe similar methods for using helium in ultrasonic applications in 6,375,931 and a method of administering contrast agents in MRI imaging was found in 6,963,769 but nothing combining the two.

In the current design, a modified MRI-1 Ventilator manufactured by CWE, Inc. is used in combination with a homemade motor-syringe pump. In the setup currently used, any MRI compatible ventilator could be used. Such units can be found from Magmedix, Inc., Omni-Vent, and Datex-Ohmeda, to name a few.

§6 Design Alternatives

§6.1 Design 1: Linear Actuators

The first design our team considered incorporates linear actuators in order to drive the inhalation breath of the rat and deliver oxygen and helium in the previously described ratio. While this design still incorporates the two one-way check valves for each syringe as well as the passive (bag) gas supply, the major difference is the removal of a stepper motor and the addition of a pneumatic air supply. Figure 6 below shows the schematic layout of the linear actuator design.

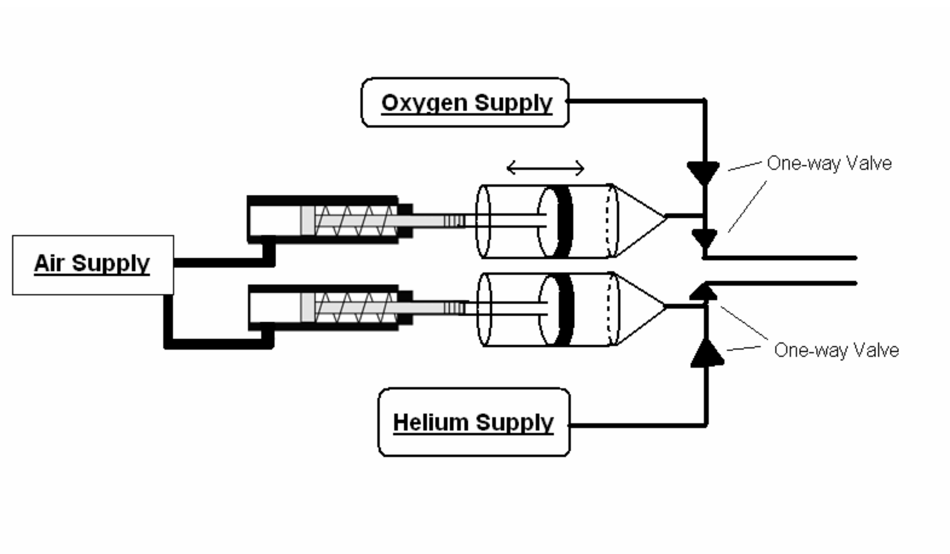

Figure 6. Schematic diagram of linear actuator design, showing additional pneumatic air supply.

We have chosen to use spring-return linear actuators. These simple actuators require only one air input to drive the piston within to its stroke length. An internal spring is then used to return the actuator to its original resting state (Figure 7). By choosing these specific actuators, we are able to reduce the number of pneumatic lines to only two (2).

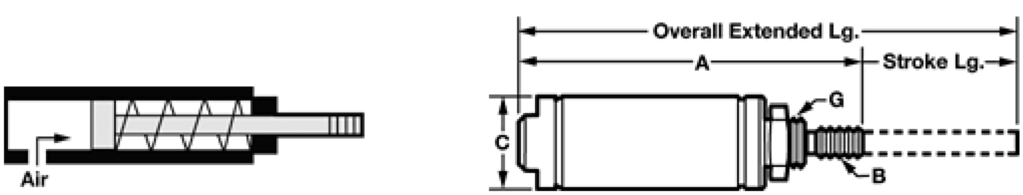

Figure 7. Left: Single air input shown with spring return. Right: Piston in resting position and stroke position shown.

Since on of the requirements of our client is to have this device be computer controlled, we must find a pneumatic air supply that can be integrated into the existing LabView program. This can be as simple as computer controlled valves installed in series with a constant pressure air supple and the linear actuators.

One of the disadvantages of using the linear actuators is that they stoke length is fixed. This means that the length is independent of the pressure and amount of air that enters the actuator. In order to obtain the 20% Oxygen to 80% Helium ratio needed, we will use different volume syringes. The syringes will not only be used to obtain the desired ratio of oxygen to helium. Since each rat has a different tidal volume of total gas delivered, the syringes will also be chosen in order to deliver this tidal volume. Since we know the linear stroke length, as well as the volume/distance ratio of the syringes, the tidal volume and gas ratio calculations will be very simple.

§6.2 Design 2: Linear Slide Tables

The second design alternative our team came up with uses linear slide tables to facilitate the injection of oxygen and helium into each breath of the rat. These linear slide tables will be driven by two (2) individual stepper motors. These motors can be independently controlled with minor alterations to the current LabView program already in use by our client. Once again, this design alternative will incorporate two (2) one-way check valves as well as the passive air supply. The schematic of this design is shown below (Figure 8).

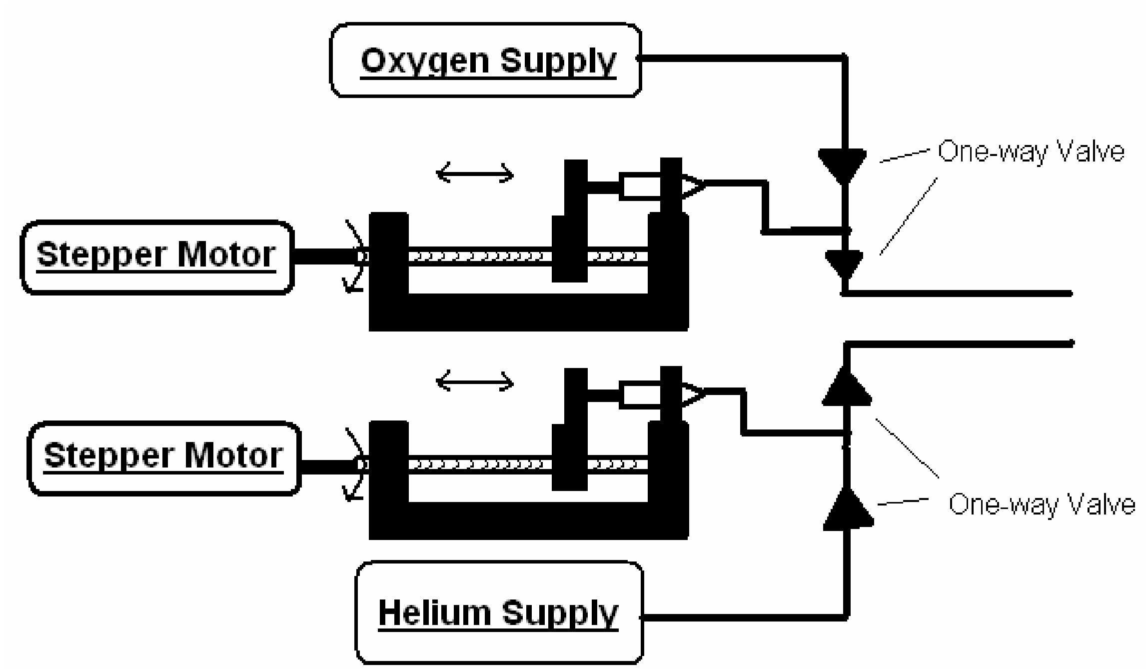

Figure 8. Schematic of the linear slide table design, including dual stepper motor control.

Linear slide tables use rotational motion, provided by the stepper motor turning and linear ball screw, and translate that rotation into linear motion on the slide (Figure 9). These slide tables are very accurate and precise. Prefabricated slide tables are available for purchase, and these tables have a known rotation per linear distance ratio.

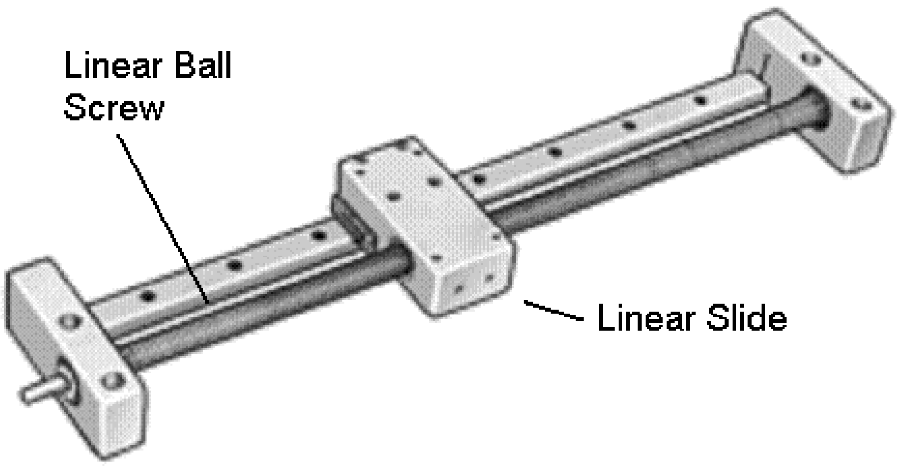

Figure 9. Linear slide table with the linear ball screw and linear slide labeled.

By using two different slide tables with separate stepper motors, this design will be able to easily control the ratio of oxygen and helium delivered to the rat by changing the amount of linear distance each table covers. We will only need to use one size of syringe, because the volume can be changed by a differing stroke length, unlike the linear actuators as described above. Furthermore, we will be able to easily control the tidal volume delivered to the rat by using the computer interface.

§6.3 Design 3: Dual Rack

Our third design proposal borrows significantly from the current design. In this design we incorporate a second rack and pinion for an additional syringe. Again, we use passive gas reservoirs and check valves to provide the O_2 and 3-He. The racks are moved by a stepper motor, which is controlled by a LabVIEW program. The current LabVIEW program should only need slight modifications to control this proposed system.

The two racks are controlled by a single stepper motor with two gears on its shaft. Each gear controls one rack, and each rack controls one syringe. One syringe delivers 3-He, and the other syringe delivers O_2. The ratio of the two gears (Figure 10) determines the ratio of O_2 to 3-He. The racks have a common gear measure, and move independent of one another. Each rack glides along two rods, and the tops are level. Figure 11 is a profile view of the rack setup without the motor or gears in place. As illustrated, the syringes sit on top of the racks.

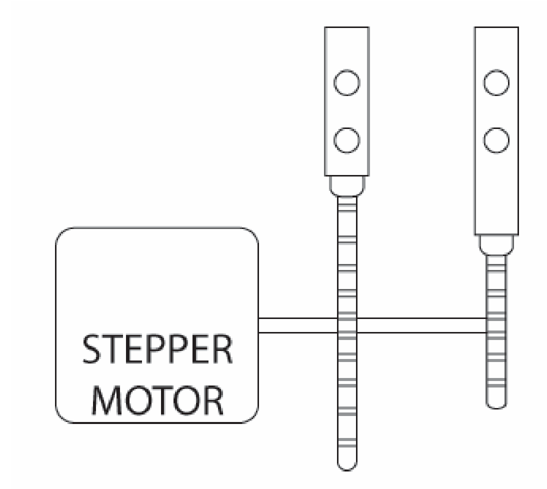

Figure 10. A front view of the stepper motor, gears, and racks. This shows the tops of the racks to be level, even with different gear sizes.

Unlike the linear actuator design, our dual rack implementation allows for a variable stroke length. This means that the amount of gas delivered by the pump can be matched to each subject's tidal volume. This design also allows us

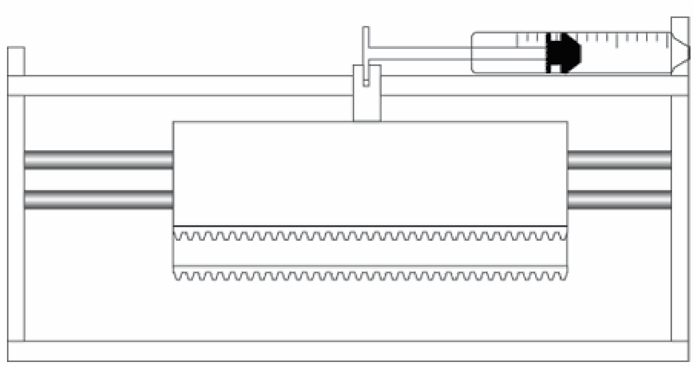

Figure 11. A profile view with the motor and gears removed. Here you can see the interface between the plunger of the syringe and the racks. Both racks are shown, the second syringe is behind the visible syringe.

to use a single stepper motor, which reduced cost, weight, and size when compared to the linear slide design. Additionally, since this design is merely a modified version of the current design, we know that it is an effective, accurate method of gas delivery, and it should only require slight modifications to the current LabVIEW interface. Unfortunately, this design still adds some unavoidable complications. As with our other proposals, a second syringe and gas supply must be added in order to control the O_2 delivery. Also, since the ratio of gas delivery is determined by the ratio of the gears, it is not easy to change this ratio. Changing the O_2 to 3-He ratio would involve changing the gears, and possibly the racks as well.

§7 Future Work

We plan to finalize and implement design three because it fits our design constraints with the least limitations. The first step in this process is to finalize the physical design (dimensions, gear sizes, syringe volumes), and develop a SolidWorks model of the apparatus. We also need to determine an appropriate stepper-motor, controller, and power supply. Then we will pick the materials, which must be (mostly) non-ferromagnetic for use in the MRI environment. With the final design and materials list, we will be able to acquire or fabricate the needed parts and assemble the device.

One of our concerns is 3-He and O_2 mixing within the dead space. This poses a potential problem for two reasons. First, if the two gasses mix significantly, or for a long period of time, we may lose the polarity of the ^{3}He, rendering it useless as a contrast agent. Second, significant mixing will destroy our desired 80% 3-He, 20% O_2 ratio, leading to asphyxiation of the subject, or low-contrast images. To test for gas mixing, we plan to image the delivery tubes of the final design while it is running. This should allow us to see any mixing as a loss of contrast in the image. A similar experiment could be performed with colored gas or smoke, but may be more difficult to see.

§8 References

1. Hedlund, LW; Moller, HE; Chen XJ; Chawla, MS; Cofer GP; Johnson, GA. *Mixing oxygen with hyperpolarized He for small-animal lung studies*. NMR Biomed. 2000 Jun;13(4):202-6. PMID: 10867697 [PubMed - indexed for MEDLINE

2. *USPTO Patent Search.* 1 Sept 2005. United States Patent and Trademark Office. 1 March 2006. < http://www.uspto.gov/patft/index.html>