Proposal Number: 2009A1882
Experiment Title: *Phase contrast X-ray imaging of lung aeration at birth*
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Beamline: 20B2

Research Purpose and Background:
The survival of premature infants is critically dependent on their state of lung maturation. Immature lungs often fail to facilitate lung aeration and gas exchange after birth and they often require respiratory assistance with a mechanical ventilator [1, 2]. Despite the life saving potential of the mechanical ventilator, it can also cause significant damage to the fragile immature lung. This damage is thought to be due to: the high pressures required to inflate the stiff immature lungs (barotrauma), regional areas of over-inflation (volutrauma), high sheer stress trauma as areas inflate and deflate at different rates and atelectrauma due to the repeated opening and collapse of the surfactant-deficient lung [1, 2]. Our primary aim was to therefore to identify ventilation strategies that promote uniform lung aeration at relatively low airway pressures and that prevent lung collapse. We have previously demonstrated that a single sustained inflation (SI) provided for the initial breath, fully inflates the lung and reduces lung collapse [3, 4].

This experiment investigated two potentially critical elements to aid in the safe ventilation of premature infants:

1. Whether a single sustained inflation of 20 seconds could promote uniform aeration even at very low inflation pressures (we tested peak inspiratory pressures of 20, 30 and 40 cm H2O).
2. Whether the technique “Particle Image Velocimetry” (PIV) [5] could be used to detect regions of high sheer stress injury in the lung, by comparing the velocity vectors with molecular markers of lung injury.

Experimental/Analytical Method:
Propagation-based phase contrast X-ray imaging and plethysmography were used simultaneously to observe and measure the patterns and rate of lung aeration in each of these groups [6]. Images were recorded in Hutch 3 of beamline 20B2 using a 24 keV monochromatic X-ray beam with a source-to-object distance of ~210 m and an object-to-detector distance of 3.0 m. Image acquisition was gated with the ventilation cycle using a Hamamatsu CCD camera (C9300-124F21) mounted with a fibre-optic taper. Figure 1 illustrates the experimental setup.

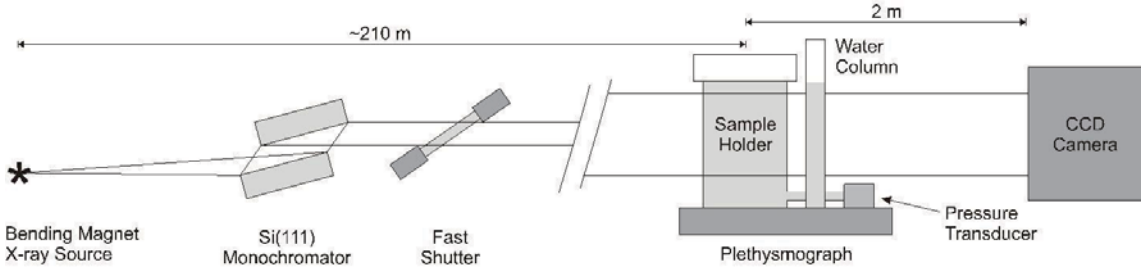

Figure 1. Experimental setup for propagation-based phase contrast imaging of newborn

rabbit pups in a water-filled plethysmograph.

Research Results:

Analysis of the data is still ongoing, however, our preliminary results suggest that:

1. The single sustained inflation of 20 seconds was not able to induce lung aeration at the low peak inspiratory pressures of 20 or 30cm H2O, although it was able to induce lung aeration at 40cm H2O. This suggests that a critical opening pressure is likely to exist in the immature lung and that a sustained inflation is not sufficient to overcome that critical opening pressure.
2. The technique of PIV has been applied to images of rabbit pups ventilated while lying on their sides. Ventilation while lying on the side causes the upper lung to inflate rapidly, which is more likely to induce sheer stress forces compared to the lower lung that inflates slowly (see Figure 2). The image analysis component of these experiments has been initiated and is currently ongoing. Following ventilation for 30 minutes on the side, the upper and lower lungs were collected for molecular analysis of the levels of known markers of ventilator-induced lung injury; this analysis is still in its early stages.

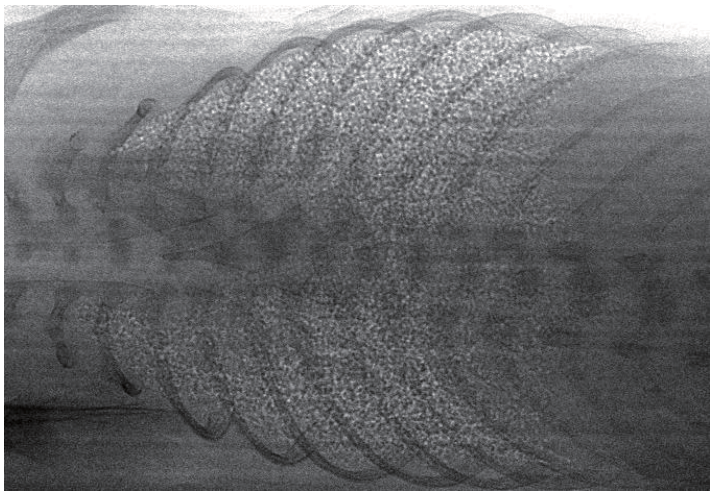

Figure 2. Side ventilation of a premature rabbit pup.

These experiments have identified ventilation strategies that are likely to reduce lung injury in preterm infants and are enabling us to identify those that are likely to promote lung injury. In addition, the technique development that we have been performing on PIV, has provided some very exciting preliminary data. When that data is compared to molecular and histological data it will provide convincing evidence that it is powerful tool for analysing defects in lung movement.

Current and Future Issues/Challenges:

None

References:

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Status of Publication and Patent:

Upon completion of the analysis of these experiments the results will be prepared for submission to peer-reviewed journals (e.g., *Journal of Applied Physiology* and/or *Pediatric Research*).

Keywords and Annotations:

Phase Contrast Imaging; Lung Imaging; Lung Development.