Measuring the Rate and Pattern of Lung Aeration at Birth

Survival at birth is critically dependent upon the ability of the lung to initiate air-breathing and take over the role of gas exchange. Before birth, the future airways of the lungs are liquid-filled and gas-exchange occurs across the placenta, whereas at birth the lungs must be cleared of liquid to allow the entry of air and the onset of gaseous ventilation [1]. However, a thin film of liquid remains to protect the inner surface of the lung from desiccation, leading to the formation of an air/liquid interface and the creation of surface tension within the lung for the first time. As a result the process of lung aeration markedly alters the distribution of force within lung tissue which initiates many changes in lung physiology allowing it to become the sole organ of gas exchange [2]. For instance, lung aeration and the onset of pulmonary ventilation is closely associated with a dramatic increase pulmonary blood flow (PBF) at birth and closure of vascular shunts that allow blood to by-pass the lungs during fetal life [2]. Thus, at birth, lung physiology markedly changes in order for it to assume the role gas-exchange and, therefore, it is not surprising that respiratory failure at birth is the greatest cause of morbidity and mortality in newborn infants [3].

Despite the fundamental importance of lung aeration to survival at birth, little is known about it because until recently, lung aeration could not be measured. As a result, the factors that determine the rate and pattern of lung aeration are unknown, although this information is particularly important for the resuscitation and ventilation of infants that are born preterm, as these infants often suffer from air way liquid retention. The application of phase contrast X-ray imaging has enabled us to observe and measure the rate and pattern of lung aeration at birth. Phase contrast X-ray imaging utilizes refractive index variations (phase information) in addition to conventional absorption information to greatly improve image contrast of the lung [4,5]. The air-filled lung is unique in that it is predominantly comprised of air (~80% by volume), surrounded by thin tissue structures (predominantly water), providing a marked transition in refractive index between airways and surrounding tissue structures. When X-rays pass through weakly absorbing tissues such as the lung, phase shifts are induced by the refractive index changes between air and tissue, causing a change in the direction of propagation which can be rendered visible by several methods [4]. The most simple is propagation based phase contrast imaging (PBPCI) where a gap between the object and detector allows the phase shifted wavefronts to interfere with adjacent waves producing strong edge enhancement [4]. Air-tissue interfaces contrast strongly using this technique (Fig. 2), making the air-filled structures of the lung visible [5]. As the fetal lung is liquid-filled it is not visible using phase contrast X-ray imaging, but rapidly becomes visible as the lung aerates after birth.

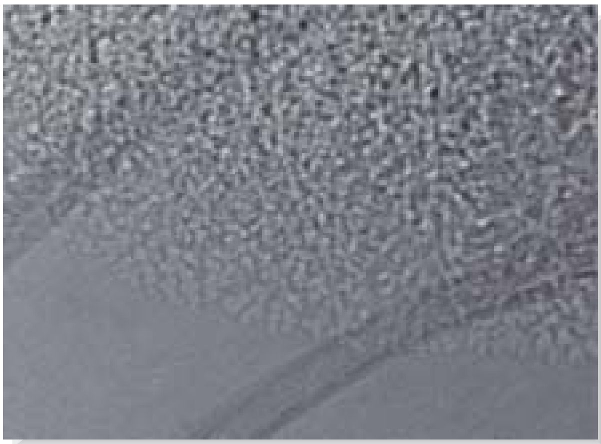

Fig. 1. Enlarged image of the peripheral margin of the lung from a newborn rabbit pup at 1 hr after birth; basal lobe of the right lung. Note that the small, terminal respiratory units are clearly visible.

Rabbit pups were delivered by Caesarian Section and were imaged either before they had taken a breath or at fixed time intervals after birth; the time points included <1 min, 3 min, 5 min, 15 min, 30 min, 1h and 2h after birth. We found that phase contrast X-ray imaging was able resolve the terminal respiratory units at the outer margins of the lungs in extraordinary detail (Fig. 1); in more medial regions, overlying air-filled structures greatly increase the complexity of the image, giving it a “speckle” appearance. In separate pups, we collected multiple images at 1-10 sec intervals for ~30 minutes after birth and measured respiratory activity from birth using a plethysmograph (Fig. 2), providing detailed information on breathing patterns after birth. Figure 3 shows the time-related changes in lung aeration that can be demonstrated using this technique. Our observations demonstrate that the pattern of lung aeration is very

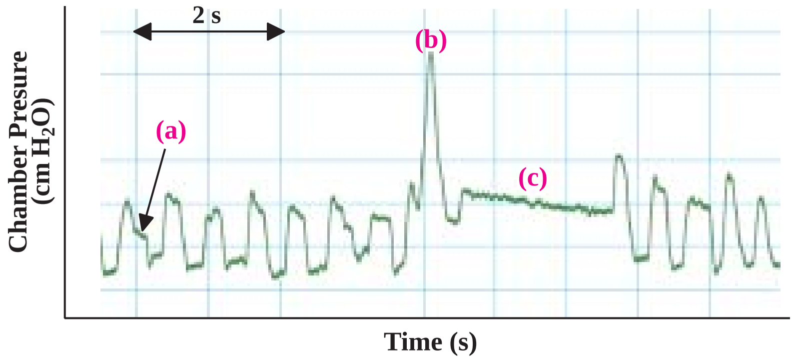

Fig. 2. Physiological recording of a newborn rabbit pup at 1 hour of age using a water-based plethysmograph. Note that expiratory braking **(a)**, deep inspiratory efforts **(b)** and breath holds **(c)** are a common feature of neonatal breathing. It is likely that significant lung aeration occurs in response to respiratory activities depicted, for example by **(b)**.

dependent upon body position and is heavily influenced by respiratory activity. Using suitable phase retrieval algorithms, we can calculate the projected thickness of the lungs from a single image allowing us to calculate the increase in air volume with time; plethysmograph recordings will be used to valid these calculations.

In conclusion, the techniques we have developed allows us to simultaneously measure respiratory activity while imaging lung aeration from birth. In future experiments we will determine the factors that determine the rate and pattern of lung aeration.

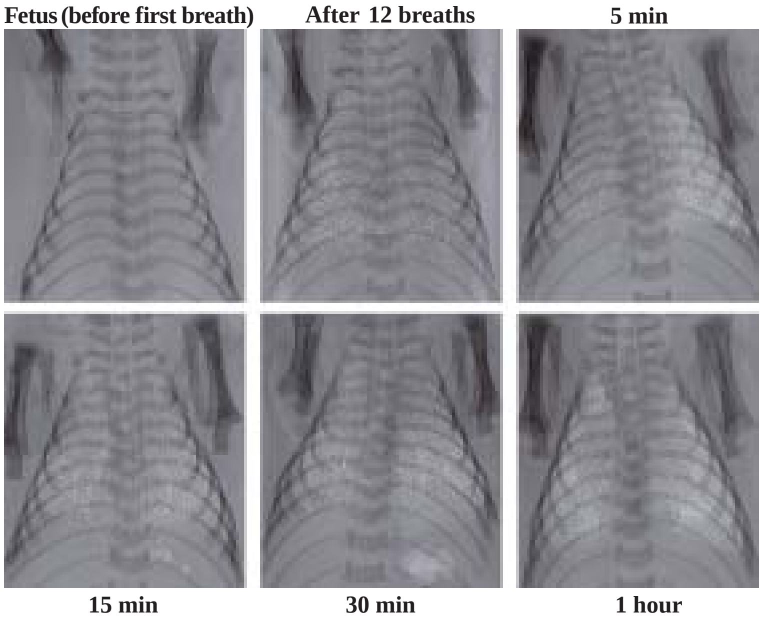

Fig. 3. Phase contrast X-ray images of rabbit pup lungs at selected times after birth.

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