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Abstract—The aim of this feasibility study was to determine whether the measurement setup and study protocol were able to show the effect that lung disease, body position and different levels of positive end expiratory pressure (PEEP) have on lung function. By means of a motorized rotation table and gravity sensors six pigs were rotated in steps of 30° from left to right lateral position. Regional ventilation distributions, measured by electrical impedance tomography (EIT), oxygenation and compliance measurements were performed at each position. Both, experimental and measurement setup as well as the parameters chosen to characterize lung function appear suitable for analyzing the effects of PEEP and rotation in healthy and injured lungs. The initial results show that the distribution of regional ventilation was highly gravity-dependent especially in sick lungs. Furthermore lateral rotation showed significant recruitment effects on previously collapsed lung tissue as witnessed by the increases in oxygenation at all PEEPs.

Keywords—EIT, electrical impedance tomography, lung function mechanical ventilation, oxygenation, PEEP, positive end expiratory pressure, rotation, recruitment, sensors.

I. INTRODUCTION

The therapeutic role of lateral rotation and prone positioning during mechanical ventilator support of patients with severe lung injury has been a matter of much debate [1]. Although most clinical trials have failed to show a clear beneficial effect of prone positioning on outcomes [2]–[4], a recent study in patients with severe lung injury showed that an early application of prolonged prone-positioning sessions significantly decreased 28-day and 90-day mortality [5]. However, the pathophysiologic and therapeutic mechanisms behind the effectiveness of position therapy remain unclear. Most parameters such as lung mechanics and blood gases used in clinical practice describe lung function only globally, but do not allow insights at a regional level.

Electrical impedance tomography (EIT) is a novel method to investigate and monitor regional lung function and heart activity. For this purpose, 32 sensors are placed around the thorax. Weak alternating currents are applied via two of these sensors and the resulting potentials are measured at the remaining sensors. From the measured voltages, sequences of real-time images are calculated which show the distribution of electrical impedance within the body [6] representing organ function rather than structure. It has been shown that intrathoracic impedance changes with ventilation [7]–[10] and the cardiac cycle [11]. The signals caused by the breathing lungs are about 10 times stronger than that caused by the beating heart. Therefore, EIT has been proposed for measuring regional ventilation rather than cardiac function within the human thorax. Unlike traditional medical imaging methods such as computer tomography, EIT imaging is non-invasive and can thus be employed continuously right at the bedside.

The distribution of ventilation depends on the lung’s condition, body position [12], [13] and on the positive end expiratory pressure (PEEP) [14]–[17] applied. Turning from the supine to the right lateral and the left lateral position, Riedel et al. [13] showed in 10 healthy subjects that the regional distribution of ventilation changes significantly with body position. They also showed that the gravity-dependent lower part of the lung is ventilated more than the non-dependent upper lung. Blankman et al. [17] showed in patients after cardiac surgery that ventilation moves towards the non-dependent lung when decreasing PEEP from 15 cmH₂O to 0 cmH₂O.

The aim of this feasibility study performed in six pigs, three with healthy lungs and three with acute lung injury, was to determine whether the measurement setup and study protocol were able to show the effect that lung disease, body position and different levels of PEEP have on global lung function and particularly on the fraction of ventilation delivered to either lung.

II. METHODS

A. Study design

The study protocol was approved by the Ethic Committee of Fundación Jiménez Díaz research institute. Acute lung damage was induced by repeated saline lung lavage for surfactant depletion and subsequent 2 hours of injurious mechanical ventilation to establish a two-hit ventilator induced lung injury model. All pigs were placed in the supine position at 0°, and were then rotated in steps of 30° in a clockwise direction until +90° and back to 0°, the same procedure was
then repeated in a counter-clockwise direction until -90° and back to 0° (for details see Fig. 1). The exact rotation of the subject was measured with an accelerometer positioned on the subject’s sternum. To ensure stable recording conditions no data were obtained during the first 2 of 3 minutes at a given angle. Baseline ventilation was performed with a tidal volume of 6 ml/kg in a volume controlled mode, at a respiratory rate of 30 breaths per min, an inspiratory to expiratory ratio of 1:2 and a PEEP of 5 cmH₂O. The fraction of inspiratory oxygen (FiO₂) was set to 0.4 for the healthy model and 1 for the lung injury model. An entire measurement sequence consisting of a total of 13 EIT recordings and arterial and mixed venous blood gas analyses was performed at each angle studied and at each of the following PEEP levels: 5, 10 and 15 cmH₂O. The order in which PEEP levels were applied was randomized. To avoid carry over effects baseline ventilation conditions were applied for 5 minutes before changing to the next level of PEEP.

B. Motorized rotation table

We used a custom-built motorized table (Guido Kübler GmbH, Bobingen, Germany) to rotate the animal to the predefined angles (Fig. 2c). The table has two linear actuators (MAX30-A200415CS10F, SKF Group, Gothenburg, Sweden) and one DC motor (403.957, Valco, Germany). In contrast to tables with only one motor, our table rotates the animal concentrically around its longitudinal axis without changing the z-direction of the table or its lateral extension. Rotation of the table was controlled by a laptop via a serial communication protocol. Before starting the experiment the table was calibrated by the electronic inclinometer Incli Tronic (BMI, Hersbruck, Germany) with an accuracy of ± 0.1° at 0° and 90° and of ± 0.3° between 1° and 89°. A vacuum mattress and two belts were used to tightly fix the animals during the rotation, see Fig. 2a.

C. EIT device

EIT measurements were performed with the Pioneer-Set (Swisstom AG, Landquart, Switzerland). This device consists of a custom-built pig interface, the SensorBelt (SB) and a SensorBeltConnector (SBC) to drive the SB, see Fig. 2b. The special pig interface was made of an elastic tube (Silcolatex 7x10, Tefelex Medical, Germany) carrying 32 contact pads made of stainless steel tubing. A standard electrically non-conductive ultrasonic gel was used to reduce the impedance between these pads and the skin. Each of these pads was connected via a cable to the SB. The SB contained 32 active sensors, which were switched between a current injecting and a voltage measurement function. In order to reduce the complexity of the belt bus within the SB the 32 sensors are arranged in daisy chain architecture. Digital commands, sent by the SBC, are then used to sequentially read out all sensors. The measured analog voltages are converted into digital signals using a 14 bit analog to digital converter. The SBC is plugged into the SB equipped with an integrated 3-axis accelerometer (ADXL343, Analog Devices, Boston, MA; USA) to measure the subject’s exact body position. Gravity and the respective other accelerations were measured at 30 Hz and converted into a longitudinal and a transversal angle, to describe the rotation angle of the subject.

An electrical drive current with peak-to-peak amplitude of 3 mA and a frequency of 144 kHz was used in all measurements. 30 tomographic differential images were recorded per second. EIT-based moving images of regional ventilation were generated from the collected potential differences and the known excitation currents using a derivative of the publically available GREIT image reconstruction algorithm [18]. More information about the EIT device can be found in [19], [20].

D. EIT data analysis

During each one of the predefined study angles EIT movies were created from 20 consecutive breaths. During post hoc analysis for each pixel the impedance difference between inspiration and the preceding end-expiration was calculated which delivered the so-called tidal EIT images. From these 20 tidal images the fraction of ventilation delivered to the right and left lung was determined simply splitting the image into a right and left hemithorax.
E. Dynamic compliance

Dynamic compliance was calculated on a breath-by-breath basis using the internal flow and pressure sensors of the Open Lung Tool (Servo-i Maquet Critical Care, Solna, Sweden).

III. RESULTS

During the experiments neither technical nor medical difficulties were encountered. All devices and sensors delivered the expected data. Fig. 3 and 4 depict the percentage of ventilation delivered to the right lung, dynamic compliance and oxygenation index for the healthy and for the lung injury model. Right at the start and during the study the lungs of the supposedly “healthy” pigs presented with a wide range of mechanical and gas exchange properties ranging from fully healthy to rather sick.

A. EIT data / Ventilation distribution

At PEEP 5 cmH\textsubscript{2}O the healthy right lung received 55\% of the tidal volume and the left lung received 45\%, see Fig.3. A slight asymmetry remained at all angles returning to almost 50\% after a complete rotation sequence. At PEEP 10 cmH\textsubscript{2}O and 15 cmH\textsubscript{2}O ventilation to the right lung increased to 70\% in the right lateral positions, whereas rotation to the left side decreased right lung ventilation to 60 and 50\%, respectively.

In contrast, the injured lung showed a higher rotation-dependency, see Fig.4. Whereas in the supine position ventilation was rather equally distributed between the right (52\%) and the left lung (48\%), in the left lateral positions 78\% of the ventilation shifted to the non-dependent upper right lung reaching as much as 73\% when back in the supine position. Even the slightest rotation by 30° to the right side inverted this distribution abruptly with the right lower lung now receiving less than 50\%. Increasing and decreasing the rotation angle did not change this ventilation pattern. The distribution of ventilation between the lungs at PEEP 10 and 15 cmH\textsubscript{2}O resembled that of the healthy lungs at PEEP 5 and 10 cmH\textsubscript{2}O, but showing a slightly larger angle-dependent hysteresis in the sick lung at PEEP 10 cmH\textsubscript{2}O.

B. Dynamic compliance

The dynamic compliance in the healthy pig ventilated at PEEP 5 cmH\textsubscript{2}O remained unchanged during the entire rotation sequence but its overall level increased with PEEP 10 cmH\textsubscript{2}O from around 15 to 20 ml/cmH\textsubscript{2}O without showing a major hysteresis, see Fig. 3. During the initial leftward rotation at PEEP 15 cmH\textsubscript{2}O a marked gain in compliance was noticed which stabilized between 20 and 25 ml/cmH\textsubscript{2}O for the remainder of the study. The sick lungs showed a similar behavior however at compliance values approximately 5 ml/cmH\textsubscript{2}O lower than their healthy counterparts see Fig. 4.

C. Blood gas PaO\textsubscript{2}/FiO\textsubscript{2} ratio

At PEEP 5 cmH\textsubscript{2}O the oxygenation index PaO\textsubscript{2}/FiO\textsubscript{2} remained between 250 and 350 mmHg in the healthy lung, reached values around 250 mmHg at PEEP 10 cmH\textsubscript{2}O and did not change with the rotation angle. At PEEP 15 cmH\textsubscript{2}O PaO\textsubscript{2}/FiO\textsubscript{2} remain between 300 and 350 mmHg and did not change with the rotation angle.

The PaO\textsubscript{2}/FiO\textsubscript{2} of about 120 mmHg at 0° corresponded to a very sick lung. At PEEP 5 cmH\textsubscript{2}O, oxygenation improved with lateral rotations to both sides reaching maximum values between 250 and 300 mmHg. Rotation at PEEP 10 cmH\textsubscript{2}O opened collapsed lung units and stabilized PaO\textsubscript{2}/FiO\textsubscript{2} value above 350 mmHg showing the same behavior also at PEEP 15 cmH\textsubscript{2}O, see Fig. 4.

IV. DISCUSSION

These initial results show that the distribution of regional ventilation was highly gravity-dependent especially in sick lungs.

The function of the healthy lung at PEEP 5 cmH\textsubscript{2}O was normal and appeared rotation-independent. With higher PEEP a clear dependency on the rotation angle was revealed which reached its maximal expression at ± 60° and ± 90° and together with the upward-convex shape of the compliance curve can be interpreted as the beginning (10 cmH\textsubscript{2}O) of overt (15 cmH\textsubscript{2}O) overdistension of the respective non-dependent healthy upper lung. Thus, high PEEP in conjunction with a high rotation angle increased the heterogeneity of ventilation in the healthy lungs.

Starting from low oxygenation levels lateral rotation showed significant recruitment effects on previously collapsed lung tissue as witnessed by the increases in oxygenation at all PEEP\textsubscript{s}. PEEP 5 cmH\textsubscript{2}O, however, was not able to maintain this recruitment. Once PEEP reached 10 cmH\textsubscript{2}O it was high enough to keep the newly recruited lung units open shifting oxygenation and compliance into the normal range. Increasing PEEP further to 15 cmH\textsubscript{2}O created a lung situation similar to the one seen in the healthy lung at 10 cmH\textsubscript{2}O reflecting a stable but slightly overdistended upper lung.

V. CONCLUSION

The distribution of regional ventilation was gravity-dependent and the combined effects of PEEP and rotation angle were different in health and disease. Both, experimental and measurement setup as well as the parameters chosen to characterize lung function appear suitable for analyzing the effects of PEEP and rotation in healthy and injured lungs.

VI. OUTLOOK

In this feasibility study in six subjects we calculated the distribution of ventilation between the right and left lung, only. In the future we should also analyze the distribution of ventilation between the gravity dependent and the non-dependent lung by dividing the lung at each angle by a horizontal line perpendicular to the gravity vector. This way, the true gravity- dependency of lung function and a correlation with parameters of global lung function should become more obvious. Furthermore it would be interesting to study the local matching of ventilation and perfusion, as suggested by [21], [22], under different rotation and PEEP conditions. Therefore, regional perfusion measurements should be included in the next study protocol. Once data analysis and study protocol have been refined in the above way they should be applied in
more pigs to reveal the underlying mechanisms of gravity- and PEEP-dependency of lung function.

ACKNOWLEDGMENT

This project was funded by the “Fondo de Investigaciones Sanitarias FIS, PI10/01885.

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Fig. 3. **Healthy lung:** Percentage of ventilation delivered to the right lung, dynamic compliance and oxygenation index $\text{PaO}_2/\text{FiO}_2$ are plotted for different body positions and PEEP level. Small arrows indicate the measurement sequence. Representative sequence of tidal EIT images during rotation from the left (+90°) to the right (-90°) lateral position show regional ventilation where bright pixels depict a large and dark ones a low ventilation amplitude. Data are plotted for each condition for three pigs. The thin lines show the data of the individual pigs, the thick violet line represents the mean value.
Fig. 4. **Sick lung**: Percentage of ventilation delivered to the right lung, dynamic compliance and oxygenation index $\text{PaO}_2/F\text{I}_2$, are plotted for different body positions and PEEP level. Small arrows indicate the measurement sequence. Representative sequence of tidal EIT images during rotation from the left (+90°) to the right (-90°) lateral position show regional ventilation where bright pixels depict a large and dark ones a low ventilation amplitude. Data are plotted for each condition for three pigs. The thin lines show the data of the individual pigs, the thick violet line represents the mean value.
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