Chapter 9

Summary

Chapter 1

Mechanical ventilation is a mainstay in modern intensive care. It is used for the treatment of patients suffering from respiratory failure. In the nineteenth century already, doubts were raised about the safety of positive pressure ventilation. Since the 1950s extensive research showed that mechanical ventilation itself can induce or aggravate lung injury. This phenomenon is known as ventilator-induced lung injury (VILI). Animal and clinical studies on acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) have elucidated the different mechanisms responsible for VILI. The term barotrauma was introduced after the observation that high airway pressures caused air leaks in the lungs. Further research demonstrated that high airway pressures are not inevitably injurious to the lungs. High airway pressures are injurious when they cause high tidal volumes, named volutrauma. In fact barotrauma and volutrauma are linked by the pressure volume relation of the lungs. Atelectrauma describes the lung injury that is induced by repetitive opening and closing of distal lung units during the respiratory cycle. Besides mechanical forces also the inflammatory response produces VILI, this is called biotrauma. Inflammatory cells and mediators play an important role in the development of lung injury. Overspill of these mediators in the systemic circulation can lead to multiple system organ failure.

Once all these mechanisms responsible for VILI were elucidated, ventilator strategies were sought that could protect the already injured lung from additional harm. High-frequency oscillatory (HFO) ventilation is one of these lung protective ventilation strategies.

HFO ventilation delivers pressure oscillations, with a frequency between 3–15 Hz, around a constant mean airway pressure, producing small tidal volumes of around 1–2 ml/kg body weight. These tidal volumes are often less than the anatomical dead space. During HFO ventilation, the tidal volumes and associated swings in alveolar pressure are very small. When applied in a recruited lung, this approach should theoretically limit ventilator induced lung injury.

The preservation of spontaneous breathing during artificial ventilation gained interest in lung protective ventilation strategies. Maintenance of spontaneous breathing in mechanically ventilated patients has several beneficial effects. Spontaneous breathing augments ventilation perfusion matching and cardiopulmonary function, reduces sedative requirement and shortens intensive care stay. Current lung protective ventilation protocols therefore aim at maintenance of spontaneous breathing. Preservation of spontaneous breathing

during mechanical ventilation was not yet an issue during the development of the HFO ventilator (SensorMedics, 3100 A/B, Yorba Linda, CA, USA) in the 1970s and 1980s. In HFO ventilation, more conventional respiratory rates and tidal volumes, as in spontaneous breathing efforts, are not needed to achieve adequate gas exchange. Unfortunately, with current HFO ventilator design vigorous respiratory efforts in large pediatric and adult patients may cause pressure swings that activate alarms, interrupt oscillations, and produce significant desaturations. Initial HFO ventilation trials in adults recommended muscular paralysis for this reason.
The main objective of this thesis was to optimize the HFO ventilator design to better tolerate spontaneous breathing during HFO ventilation.

Chapter 2

When during mechanical ventilation spontaneous breathing is maintained, the mechanical ventilator and ventilator circuit impose workload to the patient. In a bench test, we investigated which factors contributed to the imposed work of breathing (WOB) in a SensorMedics 3100 A/B HFO ventilator. A computer-controlled piston-driven test lung was used to simulate a spontaneously breathing patient. The test lung was connected to a HFO ventilator by an endotracheal tube. The spontaneous breath rate and volume, tube size and ventilator settings were simulated as representative of the newborn to adult range. The fresh gas flow rate was set at a low and a high level. The imposed WOB was calculated using the Campbell diagram.
The main result of this study is that the imposed WOB can be markedly increased during HFO ventilation in pediatric and adult patients, especially at low fresh gas flow rates. This can be a good explanation for the discomfort seen in patients breathing spontaneously during HFO ventilation. The fresh gas flow rate and peak inspiratory flow are both strongly related to the imposed WOB. In the pediatric and adult simulations, the imposed WOB exceeded the normal physiologic WOB by as much as 400%. Besides, the mean airway pressure was not maintained in the breathing circuit when the inspiratory flow exceeded the fresh gas flow rate, this even led to ventilator shutdown.

Chapter 3

The low and fixed fresh gas flow rate is an important factor in the HFO ventilator design responsible for the high workload imposed to a spontaneously breathing patient. Fluctuations in mean airway pressure also impede ventilator functioning. To overcome this problem a demand flow system was developed for the HFO ventilator. Aim of the demand flow system is to compensate for changes in mean airway pressure on account of spontaneous breathing. The basic principle of the demand flow system is to increase the fresh gas flow during inspiration and to decrease flow during expiration. As a result the imposed WOB decreases. In chapter 3 a description is provided of the hardware part and the control algorithm of the demand flow system.
The hardware part of the demand flow system consists of an electronically controlled mass flow valve, proximal pressure measurement sensor with a necessary electric circuit and control and communication electronics. The control software is developed in a MATLAB/Simulink environment (The MathWorks, Natick, USA). Using a linear quadratic Gaussian (LQG) state feedback controller, the demand flow system alters the fresh gas flow in the ventilator circuit in response to spontaneous breathing.

Chapter 4

The demand flow system was first evaluated in a bench test. Again a computer-controlled piston-driven test lung was used to simulate a spontaneously breathing patient. Spontaneous breathing was simulated to represent shallow and normal to deep breathing for a large pediatric or adult patient at a normal and rapid breath rate. The Campbell diagram and pressure time product (PTP) were used to quantify the imposed work of breathing. Using the demand flow system, imposed WOB is considerably reduced. The demand flow system reduces inspiratory imposed WOB by 30% to 56% and inspiratory imposed PTP by 38% to 59% compared to continuous fresh gas flow. Expiratory imposed WOB was decreased as well by 12% to 49%. In simulations of shallow to normal breathing for an adult, imposed WOB is 0.5 J/l at maximum. A WOB level in the physiological range, approximately 0.5 J/l in adults, seems to correspond with an optimal workload for the respiratory muscles. Fluctuations in mean airway pressure on account of spontaneous breathing are markedly reduced when the demand flow system was used. Furthermore simulation of vigorous spontaneous breathing did not trigger ventilator alarms and did not lead to ventilator shutdown, when using demand flow.

Chapter 5

The breathing pattern of a subject during mechanical ventilation is highly dependent on the interaction with and characteristics of the ventilator. For that reason the evaluation of spontaneous breathing during mechanical ventilation in a bench test has important limitations. Patient ventilator interaction cannot adequately be evaluated in a bench test. Therefore the HFO ventilator with demand flow system was evaluated in an animal model of mild lung injury.
In eight pigs (47-64 kg) lung injury was induced by lung lavage with normal saline. After spontaneous breathing was restored HFO ventilation was applied, in runs of 30 minutes, with continuous fresh gas flow (CF) or the demand flow system operated in two different setups. Pressure to regulate the demand flow system was sampled directly at the Y-piece of the ventilator circuit (DFS) or between the endotracheal tube and measurement equipment at the proximal end of the endotracheal tube (DFSPROX). In the end, animals were studied paralyzed. Breathing pattern, work of breathing, and gas exchange were evaluated.
HFO ventilation with demand flow decreased breathing frequency and increased tidal volume compared with CF. Comparing HFO modes CF, DFS, and DFSPROX, total pressure time product (PTP) was 66 $cmH_2O/s/min$ (interquartile range 59−74), 64 $cmH_2O/s/min$ (50−72), and 51 $cmH_2O/s/min$ (41−63). Ventilator PTP was 36 $cmH_2O/s/min$ (32−42), 8.6 $cmH_2O/s/min$ (7.4−10), and 1 $cmH_2O/s/min$ (−1.0 to 2.8). Oxygenation, evaluated by PaO_2, was preserved when spontaneous breathing was maintained and deteriorated when pigs were paralyzed. Ventilation, evaluated by $PaCO_2$, improved with demand flow. $PaCO_2$ increased when using continuous flow and during muscular paralysis.
We concluded that in moderately lung-injured anesthetized pigs during HFO ventilation, demand flow facilitated spontaneous breathing and augmented gas exchange. Demand flow decreased total breathing effort as quantified by PTP. Imposed work caused by the HFO ventilator appeared totally reduced by demand flow.

Chapter 6

In the same series of experiments described in chapter 5, we evaluated the effect of spontaneous breathing on regional lung characteristics during HFO with the use of electrical impedance tomography (EIT). EIT is a noninvasive technique for pulmonary imaging. EIT is able to accurately describe both global and regional lung volume changes over time during mechanical ventilation. Compared to electron beam computed tomography, as an established method to assess changes in local air content, simultaneous EIT measurements correlate quite closely. EIT was used to assess: regional lung aeration and ventilation and the occurrence of hyperinflation on account of spontaneous breathing during HFO ventilation.
End expiratory lung volume (EELV) was best preserved when spontaneous breathing was maintained during HFO ventilation compared to HFO ventilation during muscular paralysis. Lung volume was predominantly preserved in the dependent lung regions. A significant shift in ventilation toward the dependent lung regions was observed in spontaneously breathing animals on HFO ventilation with DF compared to HFO ventilation and spontaneous breathing suppressed. No signs of regional hyperinflation on account of spontaneous breathing was observed with either CF or DF.

Chapter 7

Chapter 7 provides a novel approach of high-frequency oscillatory ventilation in the pediatric population. The approach is a consensus of three based on current insights in the application of high-frequency ventilation in the pediatric population.

Chapter 8

This chapter provides a general discussion. The selected approach for the development of the demand flow system is explained. A simplified description of the control algorithm for the demand flow system is provided. The major findings of the studies presented in this thesis are discussed. The concept of spontaneous breathing during mechanical ventilation is discussed based on new insights gained from recent clinical studies. Future perspectives are given.