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formulating therapy recommendations is a 'simple' model of neonatal respiration. This model includes the neonates' delay-time of a physiological reaction to an executed therapy action. Therapy recommendations are released depending on various conditions (e.g., depending on the severity of the neonate's ventilatory status, on newly available blood gas analyses, or on various time dependencies). They consist of a set of possible and necessary changes of ventilator settings. The different strategies of these changes are represented according to the degree of blood gas abnormality. We included three possible dynamics of ventilation (e.g. conservative), according to different strategies of therapy planning, in order to be able to fulfill the requirements of different physicians using the system.

Another very important feature of VIE–VENT is that in case of a poor condition of the neonate, the dynamics of ventilation is automatically set to aggressive. This represents the practical behavior at a NICU, where the physicians have to react to a deterioration of the patient as quickly and much as possible, in order to rapidly improve the situation. At this time, VIE–VENT is clinically tested at two different NICUs.

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Dynamics of Ventilation	I				
Recommendations	conservative	normal	aggressive		
react on	blood gases	breathing pattern and blood gases	breathing pattern and blood gases		
max. allowed amount of change	50 %	100 %	150 %		
changes possible every	30 min.	15 min.	10 min.		
change of max. parameters at once	1	1	2		
max. number of changes per day	3	8	24		
interval recommended between invasive blood gas analyses	24 hours	12 hours	8 hours		

Table 2: Dynamics of ventilation in the phase of weaning

5. Technical Remarks and Future Enhancements

VIE-VENT was implemented using the knowledge representation language Clips (NASA). We used forward chaining rules for representing the knowledge base. VIE-VENT is running on IBM-compatible personal computers, Apple Macintosh and UNIX-workstations.

VIE-VENT samples transcutaneous measurements and ventilator settings every 10 seconds. The arithmetic means of these 10-second data are stored every 10 minutes for further analysis.

Enhancements of VIE-VENT cover different levels. VIE-VENT represents an event-driven approach with only limited time representation. Therefore, we are currently expanding our model of artificial ventilation (the neonatal respiration) with a combination of relative and absolute time representation (e.g. "the change of the ventilator's parameter PIP was performed 10 minutes before the neonate's health condition got better", "to improve the ventilation takes longer than to improve the oxygenation").

On the other hand, we are trying to integrate VIE-VENT in the patient data management system used at the NICUs, in order to get on-line data acquisition from the patients' records, the monitor and the ventilator. This will minimize the manual data input.

Finally, we would like to enlarge our module for prediction of short and long term effects of the therapeutic strategies and develop a more user-friendly, graphical user interface.

6. Summary of VIE-VENT's Features

VIE-VENT is a knowledge-based monitoring and therapy planning system for artificial ventilation of newborn infants. A context sensitive data validation and therapy planning component were implemented according to practical clinical and textbook knowledge. VIE-VENT uses continuous and discontinuous data input from the patient's monitors, ventilators and the data management systems.

The therapy planning component is based on a combination of transcutaneous and invasive blood gas measurements and qualitative clinical observations (e.g. chest wall expansion). The background knowledge for

The oxygenation part deals with possible reactions to SaO_2 and $PtcO_2$ measurements. As pulse oximetry (for noninvasive SaO_2 measurements) is more reliable than $PtcO_2$ measurements, priority is given to SaO_2 measurements. In case of discordant results, a warning to check the sensor sites is released by VIE-VENT. The representation and the interpretation is done in analogy to the ventilation part.

4.5.2 Dynamics of Ventilation

The dynamics of ventilation is important in the phase of weaning. There are different restrictions in the case of increasing the respiratory support.

Weaning from respirator therapy is usually performed by gradually reducing the respiratory support (IMV). The rate of reduction depends on the patient's ability to perform more work of breathing and on the physician's judgment on this ability. This judgment is usually based on blood gas analyses, on the observation of the patient's spontaneous breathing effort, and on clinical experience. Moreover, psychological characteristics of the physician, such as more conservative or more vigorous behavior are involved. Therefore various weaning strategies can be chosen and should be considered in a knowledge-based system. Disregarding of such discrepancies in the weaning strategy has led to poor acceptance of previous therapy planning systems. We have tried to overcome this problem by introducing three different weaning strategies, characterized by psychological categories: conservative, normal and aggressive. These three weaning strategies are implemented in the knowledge base of VIE-VENT, and are represented in Table 2. By default, the normal strategy is used. This may be changed on user's request to a conservative or more aggressive form of weaning.

Model: Ventilation, qualitative measurements



```
percental change rate:
s1, g1 ... 10 %
s2, g2 ... 20 %
s3, g3 ... 30 %
```

Figure 3: Therapy recommendations during the phases of controlled ventilation and weaning

Explanation of abbreviation:



Figure 2: Therapy recommendations during the initial phase; SaO₂ is below target range

Rule 1:

```
if (status is therapy_recommendation) and
  (phase_of_ventilation is initial) and
  (no_invasive_blood_gas_available) and
  (SaO<sub>2</sub> is the_single_reliable_continuous_measurement) and
  (SaO<sub>2</sub> is substantially_below_target_range) and
  (chest_wall_expansion is small)
then (increase FiO<sub>2</sub> by 20) and
   (increase PIP by 5).
```

(b) Therapy recommendations during the phases of controlled ventilation and weaning.

Figure 3 shows the possible reactions to the results of transcutaneous and invasive blood gas measurements (PtcCO₂, PCO₂ and pH) in graphical form: no changes of the ventilator settings are recommended if pH or PCO₂ or PtcCO₂ are within the target range or if PCO₂ or PtcCO₂ is not known. Acidosis and alkalosis, of both respiratory or metabolic origin, will lead to the recommendation of an increase or a decrease of the rate or the MAP. The severer the problem, the greater the amount of change. This is expressed by proportional changes of the ventilator settings (e.g., for severe problems, as indicated in Figure 3 by status "s3" or "g3", the proportional amount of change is 30%). In addition, this rate is combined with the dynamics of ventilation (see chapter 4.5.2). E.g., if VIE–VENT is used in the conservative mode, only 50% of the maximally allowed amount of change will be recommended. Two most common situations of Figure 3 are documented by rules 2 and 3. This notation presents the forward chaining rules as represented in the knowledge base of VIE–VENT.

The target values of pH, PCO_2 and PO_2 for various sampling sites (e.g. arterial, venous) are listed in the transformation schemata for blood gas abnormalities. An example for venous blood gas measurements was given in Table 1.

Description of the different phases of artificial ventilation

Depending on the course of the disease, the monitoring possibilities and the therapeutic goals of ventilation, i.e., the target values of PCO_2 and PO_2 , may change. We divided the whole period of artificial ventilation into four phases: an initial phase, a phase of controlled ventilation, a phase of weaning and a phase of returning to spontaneous breathing. Transition from one phase to the next is handled by rules depending on the amount of artificial ventilation (e.g., actual ventilator setting).

During the short *initial phase*, there are only limited monitoring possibilities, when SaO_2 is the single reliable continuously measured variable. At this time, a major goal is to characterize the severity of the disease and to optimize chest wall expansion and SaO_2 .

Then follows, depending on the severity of the disease, a more or less prolonged phase of *controlled ventila*tion (IPPV), when the main respiratory work is performed by the ventilator. During this phase, the PCO_2 target values are low, aiming to decrease respiratory drive of the patient. Spontaneous breathing efforts should be suppressed by sedation or muscle relaxation if they lead to a poor interaction with artificial ventilation or to an increased oxygen consumption. If during this phase the target values of PCO_2 and PO_2 cannot be reached with reasonable ventilator settings, the target values are adapted accordingly and alternatives to the standard therapies are taken into consideration.

When FiO₂ can be reduced to a value $\leq 50\%$ and PIP to ≤ 20 mbars, *weaning* (IMV) should be started, where the patient increasingly shares the work of breathing with the ventilator. At this time, higher PCO₂ target values are accepted in order to increase the patient's ventilatory drive.

Finally, at IMV with frequencies of ≤ 10 , FiO₂ $\leq 40\%$ and PIP ≤ 15 mbars, the phase of *returning to* spontaneous breathing with positive endexpiratory pressure (continuous positive airway pressure, CPAP) and extubation should be considered.

To illustrate our system model of neonatal respiration, we give a few examples of therapy recommendations during the initial phase and during the phases of controlled ventilation and weaning.

(a) Therapy recommendations during the initial phase

Figure 2 graphically shows the possible reactions to a decreased oxygenation depending on the degree of abnormality of the SaO_2 and the actual tidal volume (VT). The VT is here estimated by the extent of chest wall expansion. The therapy recommendations during the initial phase represent a very simplified system model, because SaO_2 is the single continuously reliable measurement.

Qualitative values of "slightly" or "substantially below target range" SaO_2 in combination with a normal or excessive chest wall expansion will cause VIE–VENT to recommend an increase of the FiO₂. If the chest wall expansion is small, VIE–VENT will recommend an increase of the FiO₂ and the PIP. Qualitative values of "extremely below target range" SaO_2 in combination with excessive chest wall expansion will cause VIE–VENT to recommend an increase of the FiO₂ and the PIP. Qualitative values of "extremely below target range" SaO_2 in combination with excessive chest wall expansion will cause VIE–VENT to recommend an increase of the FiO₂ and of the frequency (f), in combination with a normal or small chest wall expansion, it will recommend an increase of the FiO₂, of the frequency (f), and of the PIP. Rule 1 gives an example of the forward chaining rule formulation of a specific therapy recommendation.

K I N D		bek s3	ow targ	etrange 2 s1	Tarç	get Ran TV	ge	above ta g1 g	arget ra	nge g3	
O F B	pO ₂	10	30	37	40	42	45	50	65	100	mode of ventilation
Ľ		150	65	55	48	45	42	40	30	20	IPPV
0	pCO ₂	150	70	60	55	50	45	40	30	20	IMV
D G A	рН	6.6	7.2	7.2	7.23	7.25	7.3	7.35	7.55	7.7	
S '					Τ						•
Explanation of abbreviation: below target range s1 slightly s2 substantially s3 extremely			TV.	Tar	get Valı	le	above g1 s g2 s g3 s	target i slightly substan extreme	range tially ely		

Table 1: Transformation schema of the degree of blood gas abnormalities

4.5 Therapy Planning

While monitoring deals with the consecutive observation of parameters of a patient, therapy planning deals with the interpretation of the neonate's status and the selection of appropriate therapy recommendations.

Every 10 seconds, VIE-VENT monitors the transcutaneous blood gases and the ventilator settings. In addition, under certain conditions (e.g., critical ventilatory status of the neonate, or elapsed time intervals) the invasive blood gases and qualitative measurements such as chest wall expansion are requested. Therapy recommendations consist of possible and necessary changes of the ventilator settings. These changes depend on the degree of blood gas abnormality and on the three different dynamics of ventilation (e.g. conservative). The therapy recommendations are not formulated every 10 seconds. The frequency of formulation depends on the neonate's ventilatory status, on newly available blood gas analyses, on a very fast change of a measurement, and on different time dependencies.

We will focus on two important parts of VIE-VENT's therapy planning architecture: the system model of neonatal respiration and the dynamics of ventilation during the weaning process.

4.5.1 System Model of Neonatal Respiration

Neonatal respiration in our system model is represented by two processes, ventilation (CO_2 elimination) and oxygenation (oxygen uptake). Ventilation is reflected by the blood tension of CO_2 (PCO_2). Ventilation is increased (and PCO_2 decreased) with an increase of the minute ventilation which is the product of the tidal volume (VT) and the ventilatory rate (frequency, f). The VT is strongly but not linearily related to the peak inspiratory pressure (PIP) and clinically to the extent of chest wall expansion. Independently of the ventilation process, the PCO_2 may be increased due to a poor pulmonary perfusion and to right to left shunting. Oxgenation is reflected by the blood tension of O_2 (PO_2). Oxygenation (PO_2) is increased with an increase of the inspiratory oxygen concentration (FiO_2) and the mean airway pressure (MAP). The MAP increases with PIP, inflation time (ti) and positive endexpiratory pressure (PEEP). Independently of the oxygenation process, PO_2 is decreased due to right to left shunting and an increased pulmonary vascular resistance which itself at least partly depends on the PCO_2 .

e.g.: the following example s	shows corresponding values	s for	cross	checking of
chest wall expansion	tidal volume	(VT)		
1 small	\leftrightarrow	VT	\leq	5 ml/kg
2 normal	\leftrightarrow 5 ml/kg <	VT	\leq	10 ml/kg
3 excessive	\leftrightarrow	VT	>	10 ml/kg

- "Calibration" of blood gas measurements

One of the benefits of VIE-VENT is the possibility to use continuously assessed transcutaneous blood gas measurements. However, transcutaneous blood gases may deviate from the more reliably but only rarely assessed invasive blood gases. Because therapy planning is essentially based on reliable data, transcutaneous measurements have to be "calibrated" against invasive blood gas measurements. Although there is no strong linear relationship between the two types of measurement, for practical reasons we decided to use a linear calibration factor (e.g. $k = (PCO_2/PtcCO_2)$; PtcCO₂ (new) = $k * PtcCO_2$ (actual)). Calibration is only done in case the qualitative values (see next section) differ by two qualitative categories.

4.4 Data Abstraction

The quantitative data of the observable system are transformed into qualitative values. The qualitative values of the variables are used in our system model of neonatal respiration. The basis of the transformation of the blood gas measurements are schemata, which represent the degree of blood gas abnormalities. These schemata are defined for all kinds of blood gases. They depend on the site of measurement (arterial, capillary, venous, transcutaneous) and the mode of ventilation (IPPV, IMV).

Our classification of the degree of blood gas abnormality (Table 1) is based on a qualitative notation, which abstracts from the quantitative value of the blood gas measurement. In principle, the middle of the table gives the expected normal value range, the target range. "TV" is the target value we are aiming to reach. The term "below target range" means that the amount of artificial ventilation is too low. The term "above target range" means that the amount of artificial ventilation (IPPV) or intermittent mandatory ventilation (IMV). For example the transformation of the venous pCO_2 value of 58 mm Hg, when the mode of ventilation is IMV will result in a qualitative value of "slightly below target range".

One advantage of using qualitative values is their unified usability in the system model, no matter of which origin they are. Adaptation to specific situations can easily be done by using specific transformation tables without changing the model of respiration.

4.2 Data Selection

The phase of data selection, often the main starting point of the monitoring task, is the process of filtering out context-relevant data for further analysis.

VIE-VENT's whole data set can be divided into continuous and discontinuous data. The continuous data are taken from the output of the feature extraction module. The discontinuous data are entered on request to the system depending on different conditions (e.g., critical ventilatory condition of the neonate, elapsed time intervals). VIE-VENT uses the following parameters:

(a) continuous data:

ventilator settings: FiO₂, f, PIP, PEEP, tI, tE, vi, ve mode of ventilation: IPPV, IMV, CPAP transcutaneous blood gases: PtcO₂, PtcCO₂, SaO₂

(a) discontinuous data:

neonate's personal description (e.g., name, sex) clinical parameters (e.g., weight, age, chest wall expansion, spontaneous breathing effort) invasive blood gases: pH, PO_2 , PCO_2 site of blood gas measurements: arterial, capillary, venous

4.3 Data Validation

The major aim of the data validation process is to arrive at reliable measurements. There are different parts of the data validation process: the checking of plausible measurements, the handling of missing values, the rather complicated process of recognizing artifacts, and the "calibration" of blood gas measurements. These four problems are discussed in the following short examples.

- Plausible Measurements

- (a) simple checking of ranges: e.g., 15 \leq pCO₂ (arterial | IPPV) \leq 130
- (b) Reliability of measurements: From the medical and technical sampling point of view, there is a welldefined priority which measurement is more reliable than another, depending on different conditions,

e.g.: arterial blood gases are more reliable than venous blood gases invasive blood gases are more reliable than transcutaneous blood gases; oxygenation: PO₂ is more reliable than SaO₂ and SaO₂ is more reliable than PtcO₂;

- "Missing Values"

A robust system has to deal with missing values. In VIE-VENT, this problem is solved in two different ways:

- (a) using a simplified system model of neonatal respiration during the initial phase when the only reliable measurement is SaO₂ (more details are given in section 4.5.1 System Model of Neonatal Respiration);
- (b) context-dependent rules applying defaults for missing values;

- Artifacts

The recognition of artifacts is a rather complicated task. An artifact is a situation where the measured values do not reflect the clinical context. Several monitors have a built-in module for recognizing artifacts, especially those arising from hardware problems. VIE-VENT therefore does not deal with artifacts handled by the monitors. VIE-VENT uses three methods for detecting artifacts:

- (a) the measurement is out of range, which is already covered in the item of checking the plausibility of measurements;
- (b) rapid oscillations or very fast changing of a single measurement;
- (c) cross relations between different measurements



Figure 1: Tasks of knowledge-based monitoring and therapy planning

4. Architecture of VIE-VENT

Our aim in developing VIE–VENT was to integrate a monitoring and a therapy planning module according to the previously described tasks (Figure 1). According to our philosophy of a practically oriented knowledge–based system, we built the various module components in analogy to the clinical reasoning process.

4.1 Feature Extraction

A feature extraction module handles the task of data storage and retrieval, and of a low-level signal processing. The monitoring module first selects the data transmitted from various devices (e.g., patient monitor, ventilator) according to its time base of 10 seconds and stores them in a temporary form. Every ten minutes, the arithmetic means of the stored 10-second-data are calculated and written in an archiving file.

For a first evaluation of VIE–VENT we used off–line data input. Currently, we are trying to integrate VIE– VENT in the existing patient data management system at the NICUs, in order to achieve on–line data acquisition. surgical ICUs. Guardian simultaneously interprets several channels of real-time data by reactively constructing and modifying its control plans, and interleaving various signal processing tasks according to their relative importance. It is a 'proof of concept' system, which was not designed for practical use.

A small number of systems was designed mainly for intelligent alarming and alarm validating (RESPAID (Chambrin, at al. 1989), PONI (Garfinkel, et al. 1988))). The major goal of these systems is a reduction in the number of false alarms.

From the practical point of view, the usability of all these systems is limited as concerns their monitoring and therapy planning components. Most systems use invasively determined blood gas measurements for therapy planning, which, however, are only discontinuously and infrequently determined. Moreover, therapy planning in a modern ICU is increasingly based on noninvasive continuous measurements of transcutaneous partial pressure of oxygen ($PtcO_2$), arterial oxygen saturation (SaO_2) and transcutaneous partial pressure of carbon dioxide ($PtcCO_2$). Another problem of the described systems is that they do not allow for individual strategies of artificial ventilation. In addition, data validation modules are simple, and reasoning about the change of parameters over time is missing. Finally, most systems were designed for adults and are therefore not suitable for neonates. Developing VIE–VENT, we tried to overcome these limitations of the existing systems. VIE–VENT is specifically designed for practical use under real–time constraints in the Neonatal Intensive Care Units (NICUs).

3. Tasks of Knowledge-based Monitoring and Therapy Planning

Artificial ventilation of patients at a NICU involves a series of tasks ranging from simple alarming to more complex therapy planning functions. Patient monitoring usually deals with the collection of selected physiological parameters (e.g. blood gases, heart rate) which are registered, displayed and compared to upper and lower limits. The exceeding of these limits usually triggers an alarm.

Knowledge-based monitoring additionally performs analysis tasks. This presupposes an existing system model (e.g., a model of human breathing) and an instantiation of the model using current data values. Data collected by the patient monitor are selected, validated and transformed into qualitative values. The latter are compared with target values derived from the system model. If discrepancies between the system model and the current values are detected, a decision about the proper action(s) has to be made (Breucker, et al. 1987; Bykat 1991). The precise practical formulation of therapy recommendations is part of the therapy planning module. This component involves the interpretation of the patient's status, the selection of an appropriate therapy and the prediction of its short and long term effects (Hayes–Roth, et al. 1989; Coiera 1993).

As shown in Figure 1, the building of a knowledge-based monitoring and therapy planning system can be divided into several steps: feature extraction, data selection, data validation, data abstraction, and therapy planning. Therapy planning consists of interpretation of the patient's status, determination of proper therapy recommendations and the short or long term predictions of the effects of a therapy. All these steps are involved in a single cycle of data interpretation.

Knowledge-based system technology may appropriately represent and organize the practical and theoretical knowledge of experienced specialists and help to overcome the suffering from information overload with continuous data selection, data validation and therapy planning (Shortliffe, 1991). Such a system should therefore be able to support the less experienced physician in the complex decision-making of patient care, and the experienced physician in handling and analysing the complex data arising steadily from the patient monitoring system. During the past decade, several knowledge-based systems were introduced to support clinicians with the monitoring of critical care patients and to assist them with diagnostic decisions and therapy planning. These systems range from simple, intelligent alarming systems to sophisticated systems for knowl-edge-based monitoring and therapy planning (e.g., ventilator management systems).

Starting up with an overview about knowledge-based monitoring and therapy planning for artificial ventilator management, we will describe the essential monitoring and therapy planning tasks which have to be performed. The main part of the paper deals with the architecture of VIE-VENT, a monitoring and therapy planning system for artificial ventilation which we developed at the Austrian Research Institute for Artificial Intelligence (ÖFAI) in cooperation with the Gottfried von Preyer Children's Hospital, the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics of Vienna's University Medical School, and the Department of Medical Cybernetics and Artificial Intelligence, University of Vienna.

2. Knowledge-based Systems for Artificial Ventilation

A pioneer work in the area of knowledge-based monitoring and therapy planning systems was the Ventilator Manager (VM) of Fagan, et al. (1980). VM was developed in the late 1970s as one of a series of experiments studying the effectiveness of the MYCIN formalism. VM was designed for an on-line interpretation of quantitative data arising at an ICU in order to manage postsurgical mechanically ventilated patients.

VMS (Boyarsky, 1987) is a ventilator therapy planning system for neonates. Its main features are a complete record keeping facility with log reports and patients' lists and a statistical trend analysis for assisting ventilator adjustment. VMS is based on an implemented algorithm representing conventional therapy for neonates with respiratory distress syndrome and offers additional features such as a graphical display of pressure waveforms and shifted oxygen dissociation curves.

VentPlan (Rutledge, et al. 1989; 1993) is a ventilator monitoring and therapy planning system which combines qualitative and quantitative techniques. It is composed of a mathematical modeling section based on equations that describe the physiology of the heart and the lung functions, of a belief network that estimates parameter values by using qualitative information, of a plan evaluator that ranks therapy plans based on a multiattribute scoring system, and of a control algorithm.

COMPAS (Sittig, et al. 1990) is a computerized advice giving system designed to assist in the respiratory therapy of patients with adult respiratory syndrome.

Arroe (1991) developed a therapy planning system for ventilating neonates. This system proposes the direction of change of the ventilator settings based on actual arterial blood gas samples and ventilator settings. It includes a continuous trend evaluation of the last six blood gas measurements.

SIMON (Uckun, et al. 1992; 1993) is a ventilator monitoring system for premature infants. It addressed two issues, which up to then had only been covered unsatisfactorily: the issue of context sensitivity, wherein the understanding of the patient's status is related to the pathophysiology of existing disorders, and other internal and external factors such as age or degree of immaturity. The other issue deals with the correctness of measurements.

The Guardian system (Hayes-Roth, et al. 1989; 1992; Ash, et al. 1993) is a real-time monitoring and therapy planning system which may be applied to respiratory and cardiovascular monitoring problems at

VIE-VENT: Knowledge-Based Monitoring and Therapy Planning of the Artificial Ventilation of Newborn Infants

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Abstract

We developed a knowledge-based system, VIE-VENT, for monitoring and therapy planning of artificially ventilated newborn infants. One of our aims was to implement clinical and textbook knowledge in VIE-VENT's knowledge base. Therapy planning is based on a combination of transcutaneous and invasively determined blood gas measurements and clinical observations. After the selection and validation of appropriate parameters, these data are transformed into qualitative values. These are used in our model of neonatal respiration for recommending therapeutic actions according to heuristic clinical rules of artificial ventilation. For the weaning process we implemented three possible strategies, which allow adapting different dynamics of weaning (conservative, normal, aggressive). VIE-VENT is specifically designed for practical use under real-time constraints in the Neonatal Intensive Care Units (NICUs).

Key words:

Knowledge-based Monitoring and Therapy Planning, Artificial Ventilation, Newborn Infant

1. Introduction

Artificial ventilation has greatly contributed to improve the mortality and morbidity of premature newborn infants (Goldsmith and Karotkin, 1988; Teberg and Hodgman, 1992). Improved patient monitoring techniques and enhanced knowledge about the pathophysiological mechanisms of barotrauma and oxygen toxicity led to the development of patient-tailored strategies of mechanical ventilation and helped to reduce harmful side effects of respirator therapy. However, the bulk of continuous information arising from complex monitoring systems creates a rising information management problem at Neonatal Intensive Care Units (NICUs).