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Model-based control of mechanical ventilation: design and clinical validation

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Background. We developed a model-based control system using end-tidal carbon dioxide fraction ($F_{E'CO_2}$) to adjust a ventilator during clinical anaesthesia.

Methods. We studied 16 ASA I–II patients (mean age 38 (range 20–59) yr; weight 67 (54–87) kg) during i.v. anaesthesia for elective surgery. After periods of normal ventilation the patients were either hyper- or hypoventilated to assess precision and dynamic behaviour of the control system. These data were compared with a previous group where a fuzzy-logic controller had been used. Responses to different clinical events (invalid carbon dioxide measurement, limb tourniquet release, tube cuff leak, exhaustion of carbon dioxide absorbent, simulation of pulmonary embolism) were also noted.

Results. The model-based controller correctly maintained the setpoint. No significant difference was found for the static performance between the two controllers. The dynamic response of the model-based controller was more rapid ($P<0.05$). The mean rise time after a setpoint increase of 1 vol% was 313 (SD 90) s and 142 (17) s for fuzzy-logic and model-based control, respectively, and after a 1 vol% decrease was 355 (127) s and 177 (36) s, respectively. The new model-based controller had a consistent response to clinical artefacts.

Conclusion. A model-based $F_{E'CO_2}$ controller can be used in a clinical setting. It reacts appropriately to artefacts, and has a better dynamic response to setpoint changes than a previously described fuzzy-logic controller.

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During anaesthesia, carbon dioxide production varies. Thus, the minute volume has to be adjusted to maintain end-tidal carbon dioxide fraction ($F_{E'CO_2}$) within acceptable clinical limits. Several options can be chosen to adjust the ventilation settings, depending on the patient's disease and the surgery. An automatic control system might relieve the anaesthetist from this continuous control work. New technologies and better modelling methods have increased interest in automatic systems in anaesthesiology.[1] In 1996, we compared the performance of fuzzy-logic control of $F_{E'CO_2}$ with manual ventilation control and found that fuzzy-logic feedback control was reliable.[2] Fuzzy-logic systems use a rule-based method to control a process without an explicit mathematical model of the input–output relationship. An important disadvantage of fuzzy-logic control, however, is its limited transparency. In particular, the steps leading to correction of the error with respect to the setpoint are not easily understood because of the complex interaction of many rules. Optimal adaptation to individual needs is therefore difficult. Fuzzy-logic rules and their interactions are developed empirically and depend on the expertise of those who develop them. In contrast, model-based control uses scientifically established mathematical models derived from known physiological processes. This makes the controller more transparent so that *a priori* information (not available to the fuzzy-logic controller) can improve dynamic performance and optimize individual responses.

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We designed a new model-based controller for mechanical ventilation, applied it clinically and studied the response to artefacts. We assessed setpoint precision and dynamic behaviour and compared this with a fuzzy-logic controller presented by Schäublin and colleagues.[2] We expected the new device to be as stable and have a better dynamic response.

Methods

After local ethical approval and with the patients' written informed consent, 16 ASA physical status class I or II patients were studied. They were aged 18–60 yr, BMI was 15–30 and they were scheduled for elective general anaesthesia under mechanical ventilation. We excluded patients with chronic obstructive pulmonary disease and patients undergoing emergency, pulmonary or intracranial surgery, and operations lasting less than 2 h.

The patients were given omeprazole 40 mg orally the evening before surgery and premedicated with midazolam 7.5 mg orally 1–2 h before surgery. Anaesthesia was induced with propofol 2 mg $kg^{-1}$and fentanyl 0.3 μg kg^{-1} i.v. followed by a continuous infusion of propofol and remifentanil according to clinical needs. A dose of mivacurium 0.3 mg kg^{-1} was given using an Asena-GH™ pump and the trachea was intubated. Oesophageal temperature was measured and kept above 35 °C using a forced air warmer blanket. Standard measures during the study included: invasive continuous and non-invasive intermittent systolic, diastolic and mean arterial pressure, continuous ECG, heart rate, FE'_{CO_2}, ventilatory frequency (f), tidal volume (V_T), minute volume (MV), transcutaneous peripheral oxygen saturation, peak (P_{Peak}) and plateau airway pressure, inspired oxygen fraction, bispectral index and neuromuscular blockade monitoring using electromyography.

The FE'_{CO_2} was measured at the mouthpiece by sidestream infrared spectrometry (Dräger Medical AG, Lübeck, Germany), calibrated according to the manufacturer's instructions. This gave an input signal for the automatic ventilation controller. Normoventilation was defined as FE'_{CO_2}=4.5% (35 mm Hg), hyperventilation as FE'_{CO_2}=3.5% (28 mm Hg) and hypoventilation as FE'_{CO_2}=5.5% (42 mm Hg). All patients were initially normoventilated. After reaching the target FE'_{CO_2} and having maintained a stable measurement period of at least 15 min, the setpoint was randomly changed to either hyperventilation or hypoventilation (1 vol% (7 mm Hg) setpoint change respectively). To assess the dynamic performance of the controller, the setpoint was changed by 2 vol% and 1 vol% steps until the end of the operation, maintaining a setpoint for at least 15 min. Manual control of ventilation was re-established for the end of anaesthesia. All monitoring data were digitized every 5 s and stored on a hard disk.

Mathematical model and controller design

The physiological model was derived from Chiari and colleagues.[3] They presented a comprehensive model of oxygen and carbon dioxide exchange, transport and storage in the adult human that gave realistic responses under different physiological conditions. The model had three compartments (lung, brain and body tissue) with corresponding mass-balance descriptions including compartment volume, gas exchange and metabolic production. For the controller design, the model was simplified by assuming constant cardiac output and constant oxygen saturation in arterial and venous blood, so that carbon dioxide dissociation curves were not affected by oxygen saturation.[4] This gave a model that was considered sufficiently descriptive for closed-loop control purposes. A simplified schematic structure of the controller is shown in Figure 1.

Based on the physiological model, the controller included an observer system to predict the end-tidal fraction as well as the non-measurable compartmental concentrations. In case the measured input signal was transiently invalid because of sensor or clinical artefacts, the controller would switch to the predicted FE'_{CO_2} (FE'_{CO_2}pred) from the physiological model instead of the measured FE'_{CO_2}, to increase the safety and applicability of the controller in routine practice.

The desired MV was calculated by the controller every 5 s. Algorithm J was developed to translate this value into appropriate values of f and V_T for the ventilation system. An upper constraint on P_{peak} and desired settings for ventilatory frequency f_D and tidal volume V_{TD} was set by the anaesthetist to account for different patient features. When P_{peak} was reached, f was automatically increased, thus V_T decreased and P_{peak} was reduced.

Observer-based feedback systems are generally less sensitive to variation and therefore the controller could be tuned more aggressively than standard proportional-integral-derivative controllers. By adding an integral action (k_I), steady-state errors could be minimized. The controller was set up on a real-time control platform interfaced with a modified Cicero anaesthesia workplace (Dräger Medical AG, Lübeck, Germany).

Performance analysis and statistics

Controller performance was assessed by comparing the measured FE'_{CO_2} values (the controlled variable *Cm*) and the preset FE'_{CO_2} reference values (*Cr*) and calculating eFE'_{CO_2} as the difference between the FE'_{CO_2} reference value and the measured FE'_{CO_2} value. To assess the setpoint precision, the variables listed below were calculated for each patient for all setpoint values of the ventilation pattern (normo-, hyper- and hypoventilation) for the period of 10 min before changing to the next setpoint. The first two variables were defined as in the previous group with fuzzy-logic control,

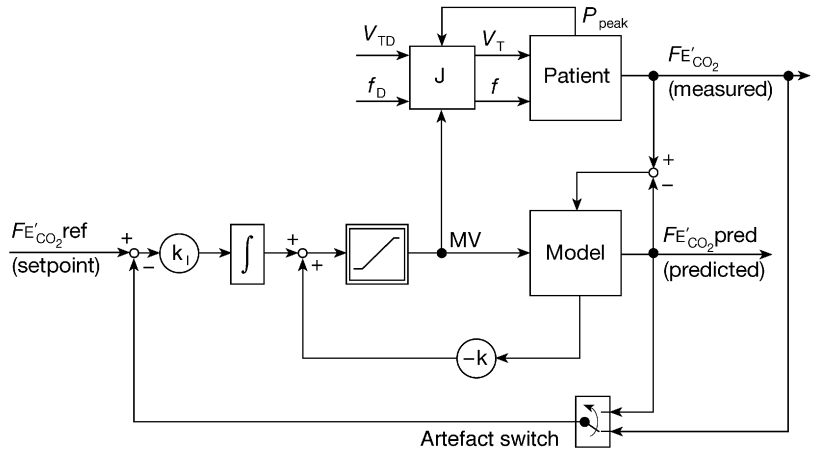

Fig 1 Simplified structure of the controller with patient, model (observer system), state feedback control vector (k), additional integral part (k_I), minute volume (MV), peak airway pressure (P_{peak}), measured $F_{E'CO_2}$, predicted $F_{E'CO_2}$ ($F_{E'CO_2}$pred) and setpoint reference $F_{E'CO_2}$ ($F_{E'CO_2}$ref), algorithm block (J) with additional inputs from the anaesthetist for desired respiratory frequency (f_D) and tidal volume (V_{TD}).

whereas variables 3–7 were calculated for the model-based control group only:

(1) MD, the mean deviation from setpoint (MD=mean $eF_{E'CO_2}$) as an indicator of the bias of the control.

(2) MDS, the standard deviation of $eF_{E'CO_2}$ as an indicator of the stability and range of deviation of the control.

(3) MAD, the mean absolute deviation from setpoint resulting in Equation 1 for subject *i* as an indicator of inaccuracy of the control, where Cm_{ij} and Cr_{ij} represent the *jth* measured and reference value for the *ith* subject, respectively.

$$MAD_i = \frac{1}{N_i}\sum_{j=1}^{N_i}\left|Cm_{ij} - Cr_{ij}\right| \qquad (1)$$

Additional measures as proposed by Varvel and colleagues[5] for the evaluation of the prediction performance of computer-controlled infusion pumps and also used to assess setpoint precision of feedback systems,[6 7] were calculated.

(4) MDAPE, the median absolute performance error, an indicator of precision or inaccuracy of the control in subject i.

$$MDAPE_i = median\left\{\left|PE_{ij}\right|, j = 1,....,N_i\right\} \qquad (2)$$

where PE_{ij} is the performance error calculated as the weighted difference between measured and reference values (Equation 3) and N_i is the number of performance errors in the *ith* subject.

$$PE_{ij} = \frac{Cm_{ij} - Cr_{ij}}{Cr_{ij}} \times 100 \qquad (3)$$

(5) MDPE, the median performance error, indicator of bias of the control in subject *i*, including the signs of the errors (Equation 4).

$$MDPE_i = median\left\{PE_{ij}, j = 1,....,N_i\right\} \qquad (4)$$

(6) The wobble is the measure of the variability of the performance errors in subject *i* (Equation 5).

$$wobble_i = median\left\{\left|PE_{ij} - MDPE_i\right|, j = 1,....,N_i\right\} \qquad (5)$$

(7) The divergence measures the time-related trend of the measured effects in relation to the targeted values.

As indicators of dynamic performance, we measured rise time (time required to move from 10% to 90% of steady state of the desired change) and overshoot (the absolute maximum value achieved, expressed as absolute value above or below the steady-state value after a step change of the setpoint).[2 8 9]

Schäublin and colleagues[2] studied 20 male and 10 female ASA class I–III patients (mean age 47 (range 12–84) yr; weight 67 (41–93) kg), during general anaesthesia for elective surgery. Anaesthetic management except ventilation was according to usual practice. They imposed two step changes from a target $F_{E'CO_2}$ of 4.5 to 5.5%, each step lasting at least 20 min. The sequence of the two steps done manually and by the fuzzy-logic controller was chosen randomly. They measured static performance, using indicators 1 and 2 above, for each individual in the last 10 min of each step. Dynamic performance was assessed as above.

The patients in the current clinical trial were compared with this historic control group using Student's *t*-test. $P<0.05$ was considered significant using a power of 0.8.

Results

Out of the 16 enrolled patients, one patient was excluded because copious lung secretions were a problem in the lateral position for hip surgery. The model-based group and

fuzzy-logic group are compared in Table 1. A sample data trace is shown in Figure 2.

The controller kept P_{peak} below the predefined limits throughout the trial for both steady-state and dynamic phases.

Setpoint precision evaluation

In Table 2 the groups are compared in terms of the precision measures and the ventilation values for normo-, hypo- and hyperventilation. No significant difference was found between the groups for these steady-state condition results. Measures of setpoint precision, calculated for the model-based control group only, confirm the stable performance of the model-based controller.

Table 1 Patient characteristics for model-based control and fuzzy-logic control groups. Data are mean (range)

	Fuzzy-logic group (*n*=30)	**Model-based group (*n*=15)**
Sex (F/M)	10/20	11/4
Age (yr)	47 (12–84)	38 (20–59)
Weight (kg)	67 (41–93)	66 (54–87)
Height (cm)	168.5 (153–192)	167 (156–188)
Operation type	N/A	3 orthopaedic 5 breast surgery 2 laparoscopic procedures 2 back surgery 2 abdominal plastic surgery 1 leg muscle reconstruction

Dynamic performance

The following 1 vol% (7 mm Hg) steps in $F\mathrm{E}'_{\mathrm{CO}_2}$ of the model-based control group were compared with the data from the fuzzy-logic control group: (i) 15 downward steps from normo- to hyperventilation (from 4.5% to 3.5%) or from hypo- to normoventilation (from 5.5% to 4.5%); (ii) 14 upward steps from normo- to hypoventilation (from 4.5% to 5.5%) or from hyper- to normoventilation (from 3.5% to 4.5%). The rise time in the model-based group was lower than in the fuzzy-logic group (Table 3, $P<0.05$). No difference was found in the overshoot of the controllers.

The results in Table 4 show the dynamic response for the 2 vol% step changes in the model-based group. Approach to an increased setpoint is significantly slower and generates a significantly larger overshoot compared with a decrease of setpoint ($P<0.05$).

Response to artefacts of the model-based controller (model-based group only)

Short intervals of invalid $F\mathrm{E}'_{\mathrm{CO}_2}$ measurements are seen in Figure 2 as decreases in the $F\mathrm{E}'_{\mathrm{CO}_2}$ curve. One event is shown in more detail in Figure 3 when the ventilation system was disconnected to ventilate the patient manually. As no valid measure of $F\mathrm{E}'_{\mathrm{CO}_2}$ was provided by the ventilation system, the controller switched to the (calcu-

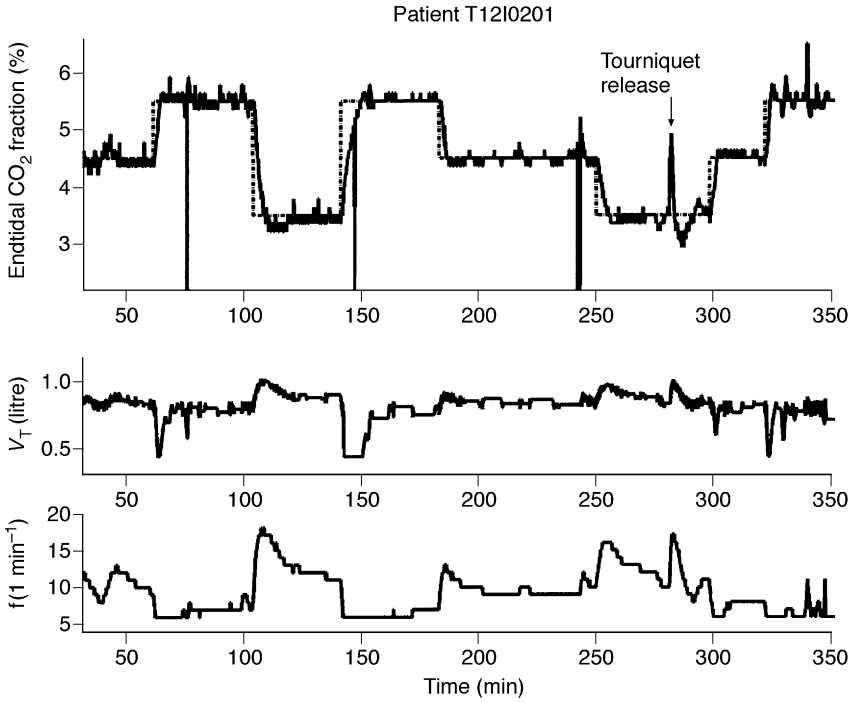

Fig 2 Example traces with artefacts during model-based control with $F\mathrm{E}'_{\mathrm{CO}_2}$ reference (dashed) and actual $F\mathrm{E}'_{\mathrm{CO}_2}$ measurement solid (top), tidal volume (V_T) (mid) and respiratory frequency f (bottom). A limb tourniquet is released at 280 min. To eliminate the accumulated carbon dioxide, the automatic feedback controller reacted by temporarily increasing the respiratory frequency and tidal volume. The decreases in the measured $F\mathrm{E}'_{\mathrm{CO}_2}$ curve show periods of invalid measurement which did not influence the controller behaviour (see Figure 3).

Table 2 Comparison of the setpoint precision and measured ventilation values of fuzzy-logic control (FLC) *vs* model-based control (MBC) for normo-, hypo- and hyperventilation. Setpoint precision is shown as mean deviation (MD) of the setpoint (MD=mean $eF\mathrm{E}'_{\mathrm{CO}_2}$) to measure bias of the control and the SD of $eF\mathrm{E}'_{\mathrm{CO}_2}$ (MDS) as a measure of the stability and range of deviation of the control. For the model-based group the additional measures mean absolute deviation (MAD), median absolute performance error (MDAPE), median performance error (MDPE), wobble and divergence were calculated. Ventilation patterns at hypo-, normo- and hyperventilation setpoints for all patients are in steady state. *f*, respiratory frequency, V_T/BW, tidal volume per kg body weight; MV/BW, minute volume per kg body weight; P_{peak}, peak airway pressure. All data are mean (SD)

	Normoventilation (4.5% or 35 mm Hg)		**Hypoventilation (5.5% or 42 mm Hg)**		**Hyperventilation (3.5% or 28 mm Hg)**	
	FLC (*n*=30)	**MBC (*n*=15)**	**FLC (*n*=30)**	**MBC (*n*=15)**	**FLC (*n*=30)**	**MBC (*n*=15)**
MD (vol%)	–0.01 (0.05)	0.00 (0.00)	0.00 (0.05)	–0.02 (0.00)	–	0.03 (0.00)
MDS (vol%)	0.09 (0.04)	0.07 (0.00)	0.11 (0.05)	0.12 (0.03)	–	0.09 (0.01)
MAD (vol%)	–	0.03 (0.00)	–	0.06 (0.02)	–	0.04 (0.00)
MDAPE (%)	–	0.0 (0.0)	–	0.0 (0.0)	–	0.0 (0.0)
MDPE (%)	–	0.0 (0.0)	–	0.0 (0.0)	–	0.0 (0.0)
Wobble (%)	–	0.0 (0.0)	–	0.0 (0.0)	–	0.0 (0.0)
Divergence (% h^{-1})	–	0.0 (0.1)	–	0.1 (0.4)	–	0.0 (0.4)
Mean *f* (min^{-1})	10.1 (1.2)	9.4 (1.2)	8.5 (0.9)	7.7 (1.0)	–	11.5 (1.0)
Mean V_T/BW (ml kg^{-1})	10.19 (1.05)	9.74 (0.59)	8.14 (1.00)	9.10 (0.73)	–	10.82 (0.74)
Mean MV/BW (ml min^{-1} kg^{-1})	103.3 (20.1)	91.8 (14.1)	69.9 (15.1)	70.6 (11.5)	–	124.2 (15.1)
Mean P_{peak} (kPa)	2.10 (0.32)	1.69 (0.30)	1.72 (0.22)	1.55 (0.30)	–	1.94 (0.26)

Table 3 Dynamic response (rise time, time required to move from 10% to 90% of steady state of the desired change) and overshoot for upward and downward setpoint changes (1 vol% or 7 mm Hg difference). Data are mean (SD). *Significant difference between groups ($P<0.05$); †significant differences between increase and decrease of setpoint ($P<0.05$)

	Fuzzy-logic group	**Model-based group**
1 vol% increase of setpoint	*n*=30	*n*=14
Rise time (s)	313 (90)*	144 (17.3)*†
Overshoot (vol%)	0.26 (0.22)	0.18 (0.12)
1 vol% decrease of setpoint	*n*=29	*n*=15
Rise time (s)	355 (127)*	177.1 (35.7)*†
Overshoot (vol%)	0.15 (0.16)	0.14 (0.00)

Table 4 Dynamic response of the model-based controller for setpoint changes of 2 vol% or 14 mm Hg (rise time and overshoot), model-based group only. Data are mean (SD). *Significant difference between increase and decrease of setpoint ($P<0.001$)

	2 vol% increase (*n*=16)	**2 vol% decrease (*n*=15)**
Rise time (s)	311 (85)*	215 (18)*
Overshoot (%)	0.39 (0.15)*	0.19 (0.07)*

lated) predicted value of $F\mathrm{E}'_{\mathrm{CO}_2}$, thus maintaining MV. When the system was reconnected, the controller switched to the measured $F\mathrm{E}'_{\mathrm{CO}_2}$, and reacted by increasing MV in response to an increased $F\mathrm{E}'_{\mathrm{CO}_2}$.

The reaction of the controller after an abrupt increase in carbon dioxide was seen after the release of a pneumatic limb tourniquet when carbon dioxide had to be eliminated with increased ventilation. This was rapidly obtained by the controller by temporarily increasing *f* and V_T (Fig. 2).

When the carbon dioxide absorbent was exhausted towards the end of the operation, carbon dioxide accumulated in the breathing system and was re-breathed by the patient. The controller reacted by increasing MV to maintain the target setpoint (Fig. 4).

Another example of fast reaction to an incident was observed when the cuff of a tracheal tube leaked. The measured $F\mathrm{E}'_{\mathrm{CO}_2}$ dropped rapidly and the controller reduced MV, triggering the low MV alarms of the monitor. The tube was replaced and no harm occurred to the patient.

The effect of a pulmonary embolism was simulated. The pulmonary shunt of the model was suddenly increased, thereby reducing the pulmonary flow and in consequence alveolar perfusion. The control system reacted by considerably decreasing MV in order to maintain $F\mathrm{E}'_{\mathrm{CO}_2}$at the preset level.

The potentially harmful consequences of the latter two incidents are discussed below.

Discussion

The clinical validation of a newly developed model-based controller for mechanical ventilation is presented. $F\mathrm{E}'_{\mathrm{CO}_2}$ is used as the controlled variable to adjust the ventilation parameters. When used with ASA I–II patients, the control system showed excellent performance and robustness in response to artefacts. The new controller was compared with a fuzzy-logic control system.[2] In this previous study, each patient was ventilated under either human or fuzzy-logic control; automatic control performed as well as human control.

Patients were satisfactorily ventilated with either control algorithm (model-based or fuzzy-logic) and no difference was found in the setpoint precision. The model-based system responds significantly faster to setpoint changes ($P<0.05$). The SD of the rise time was less in the model-based group ($P<0.05$), indicating a more consistent behaviour with step changes. This could be useful when rapid changes in ventilation are needed such as when carbon dioxide partial pressure increases after limb tourniquet

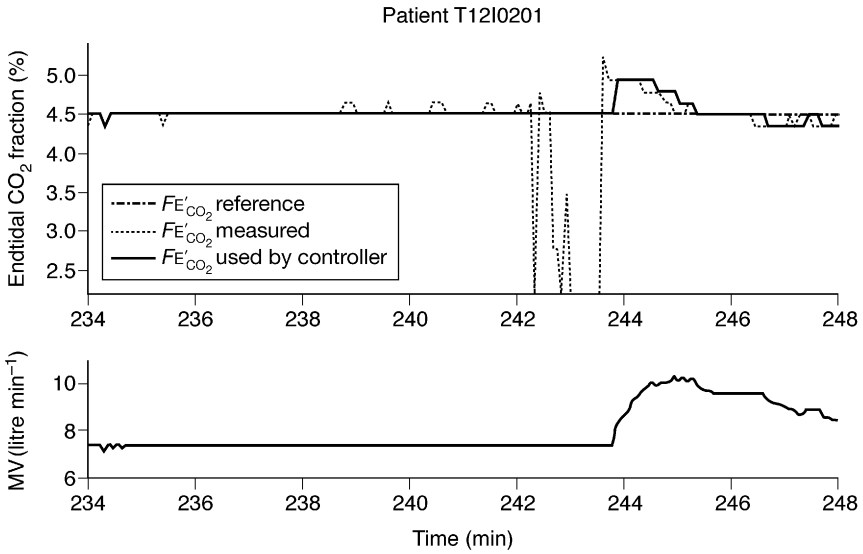

Fig 3 From 242.3 to 243.4 min of the trial shown in Figure 2, the ventilation system was disconnected and the patient was ventilated manually. The controller detected artefact measurements and switched to the (calculated) predicted $F_{E'CO_2}$ as input signal, thus maintaining constant ventilation values until the ventilation system was reconnected and accumulated carbon dioxide was washed out with increased minute volume (MV).

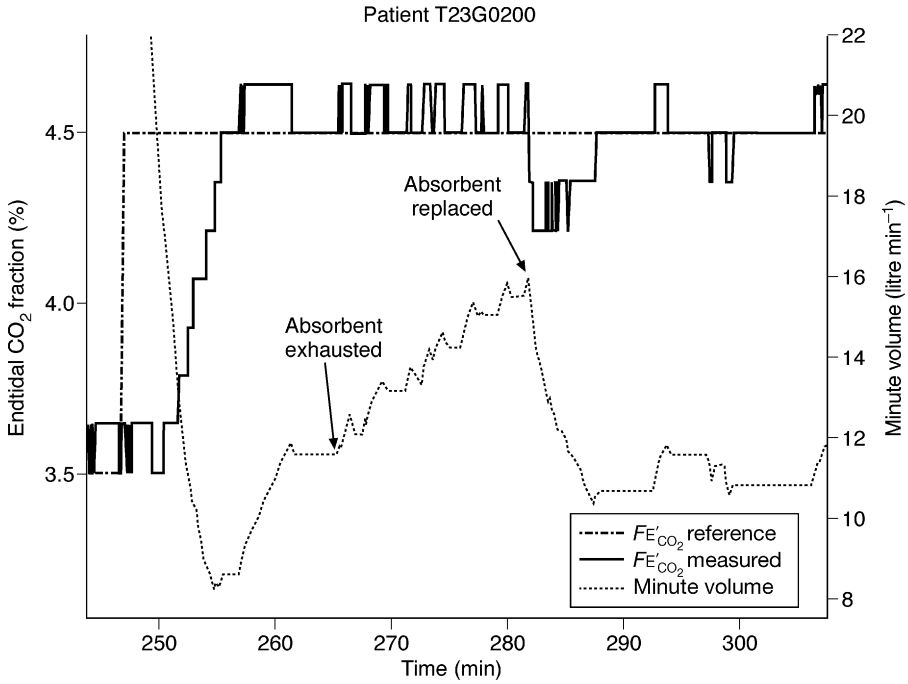

Fig 4 Reaction to exhaustion of the carbon dioxide absorbent. The minute volume was increased by the controller in order to eliminate the carbon dioxide that accumulated in the breathing system, thereby maintaining the desired setpoint of $F_{E'CO_2}$ (reference $F_{E'CO_2}$= 4.5%).

release or if ventilation has to be adapted to prevent or treat cerebral oedema.[10]

Additional measures of setpoint precision and dynamic behaviour were calculated for the model-based group. Because of the very small control bias (MD), the MAD indicator of inaccuracy showed a direct correlation to the SD of $eF_{E'CO_2}$ (MDS), confirming stability of control. However, the measures defined by Varvel and colleagues[5] and used by others[7] to estimate control quality proved to be quite insensitive to the control deviations. Except for the very small divergence values, all other values were zero. The use of median values reduces sensitivity (e.g. if the controller would maintain an exact setpoint for more than half of the time, the indicators would be zero without showing what

happened the rest of the time). In summary all these measures indicated that the controller could regulate $F\mathrm{E}'_{\mathrm{CO}_2}$ appropriately.

We found that the rise time for the model-based controller was significantly less for an increase than for a decrease for the 1 vol% steps but longer for the 2 vol% steps. This was caused by two different constraints of the controller: (i) MV was allowed to change by only 10% from one control cycle to the next. Increasing $F\mathrm{E}'_{\mathrm{CO}_2}$ means decreasing MV, in which case the actuator was reacting faster because of the 10% constraint; (ii) for the large increase the minimal MV (2.1–2.6 litre min^{-1} depending on body weight) was imposed before the 5.5% $F\mathrm{E}'_{\mathrm{CO}_2}$ was achieved, therefore dominating the rise time.

Bickford[11] described the first example of the application of closed-loop systems in anaesthesia in 1950, in animals and in man. Automatic control of $F\mathrm{E}'_{\mathrm{CO}_2}$ was suggested as early as 1974, and subsequent research showed that this could be done.[12 13] Different methods of feedback control have been developed and implemented to improve the control of anaesthesia, relieve physicians from routine activities and increase safety.[7 8 14–16] Several attempts have been undertaken to automate mechanical ventilation. Laubscher and colleagues[17] described a PI-based controller (controller with an output proportional (P) to the difference between input value and setpoint, and to the (I) integration of this difference over a certain time). Special selection algorithms were used to maintain target alveolar ventilation by selecting f and V_{T} as close to physiological needs as possible. This allowed ventilation to be adjusted according to the state of health of the patient. In this case, continuous measurements and analysis of expired carbon dioxide, airway pressure and airway flow were required.

The fuzzy-logic controller described by Schäublin and colleagues[2] had a satisfactory steady-state performance. However, its structure, based on 29 interacting linguistic rules, was very complex and hindered optimization and artefact handling. The present model-based controller performed well and also had a straightforward design based on mathematical models, which could facilitate future approval by authorities and/or official bodies. The model-based controller is 'familiar' with the behaviour of the process that it is adjusting; *a priori* information about the natural process not available to model-independent controller types such as fuzzy-logic can be used to improve dynamic performance. We have shown this was indeed the case. Furthermore, with a sufficiently general model, the controller can handle different ventilation regimens.

However, automatic controllers of mechanical ventilation cannot directly recognize dead-space ventilation, for example in the case of pulmonary embolism. With decreasing $F\mathrm{E}'_{\mathrm{CO}_2}$ because of increased dead-space ventilation, the controller would react by reducing the ventilation, thereby keeping $F\mathrm{E}'_{\mathrm{CO}_2}$ as close to setpoint as possible and this would increase arterial carbon dioxide partial pressure. This also occurred during a trial when the tube cuff leaked, which resulted in a reduced effective V_{T} and reduced alveolar ventilation. With pulmonary embolism, the controller would react to the decrease of $F\mathrm{E}'_{\mathrm{CO}_2}$ with a reduced MV, as was verified in a simulation environment. The detection of increased dead-space ventilation and/or circulatory compromise, leading to decreased carbon dioxide return, is therefore possible when monitoring MV. However, we consider an MV alarm to be less dependable in a clinical setting than an $F\mathrm{E}'_{\mathrm{CO}_2}$ alarm, because it depends on the size of the patient. To increase safety, we suggest that the controller should detect and alarm if a sudden or unexplained decrease in MV occurs in relation to patient features such as weight, height and sex. In an alarm situation, the controller could be switched to the (calculated) predicted value of $F\mathrm{E}'_{\mathrm{CO}_2}$, thus maintaining MV according to standard patterns until the anaesthetist resolves the situation and clears the alarm. The controller could also process the continuous carbon dioxide fraction and flow measurement, calculate anatomical dead space and signal changes.

Automated control in anaesthesia is increasingly studied for various input and output measurements. Because our model-based controller can maintain adequate control despite various measurement artefacts, it could serve as an example for development of robust (artefact-tolerant) controllers. Once robust control is routinely established in anaesthesia, the simultaneous use of automatic controllers of different systems (e.g. mean arterial pressure, bispectral index, neuromuscular relaxation, ventilation) could considerably relieve the anaesthetist from routine control work, allow better understanding of the interactions between the various control loops and should improve patient care. This could open new perspectives for both research and clinical use.

Both the fuzzy-logic and the model-based controller can maintain a chosen setpoint with high precision. The dynamic performance of the model-based controller was better. The responses to several artefacts showed that the model-based control is robust. This controller seems to meet the requirements for routine clinical application.

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References

1 Struys MM, De Smet T, Mortier EP. Closed-loop control of anaesthesia. *Curr Opin Anesth* 2002; **15**: 421–5

2 Schäublin J, Derighetti M, Feigenwinter P, Petersen-Felix S, Zbinden AM. Fuzzy logic control of mechanical ventilation during anaesthesia. *Br J Anaesth* 1996; **77**: 636–41

3 Chiari L, Avanzolini G, Ursino M. A comprehensive simulator of the human respiratory system: validation with experimental and simulated data. *Ann Biomed Eng* 1997; **25**: 985–99

4 Stadler KS, Leibundgut D, Wessendorf R, Glattfelder AH,

Zbinden AM. Automatic feedback control of mechanical ventilation during general anaesthesia: A model-based approach. *IFMBE Proc 2nd European Medical & Biological Engineering Conference (EMBEC 2002)* 2002; **3**(2): 1602–3

5 Varvel JR, Donoho DL, Shafer SL. Measuring the predictive performance of computer-controlled infusion pumps. *J Pharmacokin Biopharm* 1992; **20**: 63–94

6 Absalom AR, Sutcliffe N, Kenny GN. Closed-loop control of anaesthesia using Bispectral index: performance assessment in patients undergoing major orthopaedic surgery under combined general and regional anaesthesia. *Anesthesiology* 2002; **96**: 67–73

7 Struys MM, De Smet T, Versichelen LF, Van De Velde S, Van den Broecke R, Mortier EP. Comparison of closed-loop controlled administration of propofol using Bispectral Index as the controlled variable versus "standard practice" controlled administration. *Anesthesiology* 2001; **95**: 6–17

8 Asbury AJ. Feedback control in anaesthesia. *Int J Clin Monit Comput* 1997; **14**: 1–10

9 Glen JB, Schwilden H, Stanski DR. Workshop on safe feedback control of anaesthetics drug delivery. Schloss Reinhartshausen, Germany. June 29, 1998. *Anesthesiology* 1999; **91**: 600–1

10 The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Initial management. *J Neurotrauma* 2000; **17**: 463–9

11 Bickford RG. Automatic electroencephalic control of general anesthesia. *EEG Clin Neurophysiol* 1950; **2**: 93–6

12 Giard MH, Perrin F, Bouchet P, Robert D, Pernier J. [EOLE: a system for the automatic control of pO_2 and pCO_2 during artificial ventilation]. *Med Biol Eng Comput* 1983; **21**: 503–8

13 Ritchie RG, Ernst EA, Pate BL, Pearson JP, Sheppard LC. Automatic control of anesthetic delivery and ventilation during surgery. *Med Prog Technol* 1990: **16**(1–2): 61–7

14 O'Hara DA, Bogen DK, Noordergraaf A. The use of computers for controlling the delivery of anesthesia. *Anesthesiology* 1992; **77**: 563–81

15 Dojat M,.Brochard L. Knowledge-based systems for automatic ventilatory management. *Respir Care Clin N Am* 2001; **7**: 379–96

16 East TD, Heermann LK, Bradshaw RL, *et al*. Efficacy of computerized decision support for mechanical ventilation: results of a prospective multi-center randomized trial. *Proc AMIA Symposium* 1999; 251–5

17 Laubscher TP, Heinrichs W, Weiler N, Hartmann G, Brunner JX. An adaptive lung ventilation controller. *IEEE Trans Biomed Eng* 1994; **41**: 51–9