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Intelligent Generating Controller a Desflurane Concentration Value Which Helps to Decrease Blood Pressure

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Introduction: The aim of the article is to determine the appropriate concentration of desflurane to effectively counteract the increase in blood pressure resulting from surgical stress. In medical practice, this increase is often limited by using additional doses of opioid drugs. Additional medications or higher doses of those already used may adversely affect your health. During anesthesia, physician must note the use of drugs and remember them, especially those that he has recently administered, which affect his concentration. For this purpose, the authors decided to propose support for the selection of desflurane concentration so that frequent use of opioid drugs is not necessary. The authors used a system based on AI issues to accomplish this task. The learned system supports the anesthesiologist's work by imitating him.

Patients and Methods: The proposed method for selecting the desflurane concentration is based on a fuzzy controller. This system includes a learning mechanism that allows for minimizing the operating error. The main advantage of this system is the ability to build a function allowing the selection of anesthesia parameters without knowledge of the mathematical description of the process. To accomplish this task, you need an expert who will provide information in the construction of logical if-then sentences (points in space). The fuzzy controller connects the points in the consideration space appropriately, generating a hypersurface. The algorithm test was performed only by computer without the participation of patients.

Results: The operation of the proposed algorithm was verified by computer simulation. The authors of the article analyzed the compliance of the obtained results with the table provided by the expert. The desflurane concentration values obtained by computer simulation are similar to those given in the table Minimal driver error does not affect the patient's clinical response. This error results from the functions used in the fuzzy system and its settings. The results of the performance test of the proposed algorithm are presented in a time course, and it has the shape of a step function. The work proposes a function that allows you to enter the time needed for the body's reaction to reach the desired E_{tdes} level.

Conclusion: In this study, a controller was created to support the selection of the concentration of desflurane allowing for a reduction in blood pressure (resulting from surgical stress). The results obtained by computer simulation provide valuable insights for optimizing anesthesia. This system can also be used as an important simulation program for teaching purposes.

Keywords: fuzzy logic, anesthetic support, desflurane, mathematical models of desflurane

Introduction

In the Health 4.0 era, most medical processes are digitized and computer-aided, especially using intelligent predictive algorithms. Due to the specific nature of an anesthesiologist's work, computer support for his activities is important. Various models of anesthetic machines together with the staff in the operating room and other external factors negatively affect the anesthesiologist's concentration. Elimination of large doses of opioids is possible with a short-term increase in desflurane concentration. For this reason, supporting the anesthesia process is useful. The problem of supporting

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anesthesia was discussed in Manzoni and Rampazzo.[1] The authors of this article present typical problems and needs of automation, pointing to the use of a special intelligent controller operating in a closed loop for anesthesia involving the intravenous administration of anesthetics. A description of the control in anesthesia algorithm can be found in Gentilini et al.[2] An important point of this work is to indicate the possibility of using the ANFIS (Adaptive Neuro-Fuzzy Inference System) controller can be found in these studies.[3,4] The same type of driver was used by the authors of this article. Support for anesthesia using the pharmacological agent Propofol is often discussed in the literature. However, there are no scientific studies on supporting the selection of anesthetic gas concentrations. The main works that contributed to the article are in this study.[5] In the proposed solution, the quality and effectiveness of anesthesia can be increased by using additional information on the desflurane concentration value. The authors of the article determine this value on the basis of data from the vital signs monitor (*DIA* and *SYS*) and the depth of anesthesia - *BIS*. The information generated by the proposed algorithm is intended to maintain the anesthesia process so that the patient is unconscious and his blood pressure is at the appropriate level. An intelligent algorithm based on a fuzzy controller was used to perform such a task. It allows for modeling the process (anesthesia) without the need to use a mathematical description of the anesthesia process. The anesthesia support algorithm is based on expert knowledge (an experienced anesthesiologist) and is able to faithfully imitate the process of determining the concentration of anesthetic gas. The proposed algorithm is built in the Matlab computer program. The knowledge of an experienced anesthesiologist can be tabulated and arranged in natural language using logical if-then statements. To implement such a system, a fuzzy controller based on *TSK* (Takagi-Sugeno-Kang) reasoning was used. This system is built, among others, of neural networks that allow to reduce the error of the algorithm. In the case of two input variables (*DIA, SYS*) and one output variable (E_{tdes}), the intelligent controller can generate a hypersurface reflecting its operation. The algorithm must include external data (BIS parameter and arterial pressure) measured by the anesthesia machine. The BIS bispectral index is checked at the beginning of the algorithm as a conditional main loop. The hypersurface mesh points are given in the expert table and their connection results from the mechanisms set in the fuzzy controller. The output from this system is the desired desflurane concentration that allows for lowering blood pressure. The generated value (E_{tdes}) must be set manually using the desflurane evaporator knob. The fastest achievement of a given desflurane concentration is achieved by changing the fresh gas flow rate along with the change in the anesthetic gas concentration on the evaporator. Due to the fact that each patient reacts differently to pain, the authors of the article limited additional variables and created an anesthesia support model based on the ASA I group. Patients were not used in the algorithm performance test. The data needed to implement the controller was provided by an expert in the medical field. The output value (E_{tdes}) from the controller should be entered into the input of the inertia system. In the article, using a computer program, the times needed to achieve the expiratory concentration of desflurane were determined for a patient weighing 70 kg while changing the flow of fresh gases. The reaction time of the circulatory system to an increase in the concentration of desflurane depends on the individual characteristics of the patient.

Materials and Methods

Theoretical Background

From a chemical point of view, desflurane (2-(difluoromethoxy)-1,1,1,2-tetrafluoroethane) is a fluoro derivative of ethyl methyl ether with formula $C_3H_2F_6O$ (Figure 1). It is a volatile, colorless liquid.[6] Together with sevoflurane, isoflurane and enflurane, desflurane is currently one of the most common anesthetic agents. Since they are nonflammable and

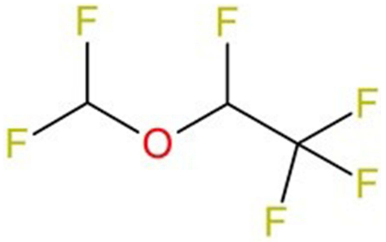

Figure 1 Structural formula of desflurane (2-(difluoromethoxy)-1,1,1,2-tetrafluoroethane).

relatively volatile, organofluorine anesthetics are in general safer than their previously used alternatives.[7] One of the most important advantages of desflurane is that it is not metabolized easily (≈10% of that seen with isoflurane), which reduces the risk of hepatitis and nephrotoxicity.[8–10] The blood–gas partition coefficient for desflurane was found to be 0.57 ± 0.04 (mean ± SD).[11] Desflurane also "washes-out" ≈2 to 2.5 times faster than isoflurane, which reduces the time necessary for recovery and makes it easier for the medical staff to control the condition of the patient.[10]

It is important to note that there are possible interactions between organofluorine agents and carbon dioxide absorbent used in anesthesiology – soda lime, which may lead to formation of carbon monoxide. This phenomenon, however, occurs at higher temperatures, when carbon dioxide absorbent contains very small amounts of water. Desflurane itself undergoes slight degradation at 80°C (0.45% per hour).[10,12–15] Since desflurane is not easily metabolized, certain amounts of this agent can be released to the atmosphere. This compound has a very important impact on the environment – desflurane is classified as greenhouse gas. Along with other organofluorine agents, it potentially damages the ozone layer. Atmospheric lifetime of these anesthetics varies from 1.4 year for sevoflurane and 21.4 years for desflurane. One of the simplest ways of minimizing the environmental pollution connected with using desflurane is to decrease maintenance flows from 4–6 L/min to 1–2 L/min.[16–19] Recently also the impact of anesthetic agents on cancer cells has been studied, proving that inhalational agents in some cases may worsen cancer outcomes.[20,21]

One of the most important factors describing the properties of an anesthetic gas is a blood-gas partition coefficient, which is connected with a solubility of a specific anesthetic gas in blood. In general, the lower the coefficient value, the faster the anesthetic gas reaches the brain and induces the desired effect in patient. It thus allows for the medical staff to control the patient's condition more easily. Moreover, worse solubility in blood also means lower amount of the gas necessary for obtaining the desired reaction. For desflurane, the partition coefficient value (at 37°C) is 0.57, while for sevoflurane and isoflurane it's 0.74 and 1.45, respectively.[11,22,23]

As shown, time and solubility of anesthetic agents are crucial factors in anesthesia. The observed phenomena can be explained using Henry's law (1), commonly known in physical chemistry.

$$p_i = x_i \times K_i \tag{1}$$

where: p_i – partial gas pressure; x_i – amount of the dissolved gas; k_i - Henry's law constant.

It states that the amount of the gas that is dissolved in a liquid is proportional to its partial pressure above the liquid. When an anesthetic agent is inhaled, its partial pressure in pulmonary alveoli increases and, according to the Henry's law, the agent is taken up by the pulmonary circulation and later delivered to the brain. A poorly soluble anesthetic agent (blood-gas partition coefficient) is delivered to the brain more efficiently and thus induces the desired effect faster. The second important factor is the pulmonary alveolar blood flow, which in most cases is equal to the cardiac output. The higher the cardiac output, the greater is the absorption of the anesthetic agent from the lungs. However, this does not accelerate the induction, since the higher uptake of the agent results is a decrease in the agent's amount in the alveoli. The last important thing is the difference in the alveolar and venous partial pressures due to the tissue uptake of the anesthetic agent. A type of tissue plays a crucial role here, since it determines the blood flow through the tissue, the blood to tissue partial pressure difference, and the blood tissue solubility coefficient.[24] All of the above factors must be considered during the actual process to reach the expected effect. This obviously sets an important task to choose the anesthetic agent correctly, as well as its flow rate.

The study was a theoretical study, the patients were not included in the study, no intervention was performed; therefore, the ethics committee approval was not necessary to obtain.

Anesthesia in the MFA Scheme

The *MFA* (Minimal-Flow Anesthesia) under combined general anesthesia consists of three basic parts: induction, conduction and awakening. The induction phase consists of a few parts – passive oxygenation with *CPAP* (Continuous Positive Airway Pressure), administration of analgesics and neuromuscular relaxants, endotracheal intubation and initiation of ventilation of fresh gas with desflurane in high-flow. After reaching the expiratory concentration of desflurane Et_{des} (end-tidal concentration) equal to the *MAC* (minimum alveolar concentration), the supply of fresh gases consisting of oxygen (Oxygenium 99.5%) and air can be reduced to a flow value meeting the *MFA* criterion (2 L/

min). In this phase, the parameters such as adequate SpO_2 oxygenation and stable hemodynamic parameters should be controlled.

The parameters which are set at startup in the respiration system are the setting of the tidal volume TV based on the relationship 6–8 mL/kg IBW (IBW- ideal body weight).[25] The important parameter is the $SpO2$ saturation measured by the pulse oximeter and its trend (plethysmographic curve) which should be kept normal. The relationship determining the supply of oxygen to tissues is defined by: $DO_2{=}CaO_2 \times CO$ (CaO_2 - oxygen content in arterial blood, CO - cardiac output) where: $CaO_2{=}\ (1.34 \times Hb \times SaO2){+}\ (0.0031 \times PaO_2)$ (Hb - hemoglobin level in arterial blood, SaO_2 - hemoglobin saturation with oxygen in arterial blood). In the equation for oxygen content in arterial (CaO_2) the oxygen partial pressure in arterial blood (PaO_2) has little effect on the value of DO_2. Achieving PaO_2 values between 90 and 100 mmHg allows to achieve 100% Hb saturation. Further increasing the PaO_2 level may cause atelect changes in the lungs. Therefore, the authors of the article maintain the saturation SpO_2 hold at the limits 95–99%. The proposed desflurane automation system sets the desired value of the flow of fresh gases and concentration anesthetic. The system controls among others these values to achieve stability of the patient. For example, in the case of a decrease in the value of SpO_2 parameter and an increase in blood pressure (BP) the proposed system to reduce vascular resistance by increasing the concentration of desflurane together with the flow of fresh gases. The FiO_2 is achieved in adequate saturation within safe limits.

The breathing respiratory component consists of the oxygen flow rate 0.5 L/min, air 1.5 L/min and desflurane. The oxygen concentration in the gas input system (in input of vaporizer) does not exceed the value of 0.4 designated by formula (0.21×1500 mL/min+1×500 mL/min)/(1500 mL/min+500 mL/min). The oxygen fraction Fio_2 in the breathing mixture in the output of the gas stream from the desflurane vaporizer it can be determined from $(0.21 \times 1500\ \mathrm{mL/min}+1 \times 500\ \mathrm{mL/min}+0_{\mathrm{desflurane}}\text{-}250\ \mathrm{mL/min})/(1500\ \mathrm{mL/min}+500\ \mathrm{mL/min}+\mathrm{Uptake}_{\mathrm{des}})$. Knowing the dependence on the concentration of desflurane $c_{\mathrm{desflurane}}{=}Flow_{des}/(flow_{main}{+}flow_{des})$ in output gas from vaporizer $0.06{=}Flow_{des}/(2000\ \mathrm{mL/min}{+}flow_{des})$ and substituting the data for MAC (Minimal Alveolar Concentration) 6 vol.% the desflurane vapor flow will be equal to 127 mL/min.[26] In the case of an oxygen uptake Vo_2 of $250\ \mathrm{mL} \times \mathrm{min}^{-1}$. The oxygen desired fraction was calculated for cardiac output (CO) 4L/min and body weight BW=70kg during anesthesia in the case of the conduction phase, about 20 minutes from the beginning of unscrewing the desflurane vaporizer in breathing circuit and is 0.31. This value is based on equation $(0.21 \times 1500\ \mathrm{mL} \times \mathrm{min}^{-1}+1 \times 500\ \mathrm{mL} \times \mathrm{min}^{-1}\text{-}250\ \mathrm{mL} \times \mathrm{min}^{-1})/(1500\ \mathrm{mL} \times \mathrm{min}^{-1}+500\ \mathrm{mL} \times \mathrm{min}^{-1}\text{-}22\ \mathrm{mL} \times \mathrm{min}^{-1}\text{-}250\ \mathrm{mL} \times \mathrm{min}^{-1})$. The value of $22\ \mathrm{mL} \times \mathrm{min}^{-1}$ is the desflurane uptake at 20 minutes in anesthesia designated for CO=4L/min and blood gas partition ratio b/g 0.42. The Figure 2a shows the desflurane uptake as a function of the different CO coefficient (4, 4.5, 5 L/min). The cardiac output varies during the procedure, therefore its analysis should be considered. The Figure 2b shows the concentration F_{iO2} of oxygen from breathing gas as a function of the different CO coefficient (4, 4.5, 5 L/min) and the concentration of desflurane.

The charts from Figure 2 were generated in Matlab software. The two curves (see Figure 2a) form the limit of variation in the uptake value of desflurane with constant cardiac output CO=const. and varying of expiration E_t (End tidal) concentration of desflurane from 6 to 7.2 vol.% (1–1.2MAC). The range of variability of uptake of desflurane is so small that it can be ignored. The most important is the value of uptake of desflurane at 20 minutes of anesthesia due to the function of tissue saturation of anesthetic. Low-flow anaesthesia starts initially with high fresh gas flows 6 L/min and then the total flow can be reduced to 2.0 L/min after 20 min. Figure 2b shows concentration of Fio_2 which depends on level of desflurane uptake and oxygen and cardiac output value ($Fio_2(CO,\ Uptake_{des,}VO_2)$).

In low-flow anaesthesia, changes in fresh gas flow ratio require a large amount of time to cause changes in the gases in the breathing circuit. With the desired values 1MAC at 20 minutes of anesthesia ($V_{desflurane}$=22mL/min), and FGF=2L/min this time is 2.53 minutes. This time is too long; therefore, the flow should be increased so as not to exceed $F_{iO2} = 30\%$. Based on the charts, it can be concluded that it is not possible to implement automatic selection of anesthesia parameters before 20 minutes after its start. Despite setting oxygen at a concentration of 40% due to the oxygen and desflurane uptake the FiO_2 concentration after 20 minutes of anesthesia will be about 30% (Figure 2b). The automation system must know the relationship between the settings of anesthesia machine and the parameters resulting from the physiological activities of the patient.

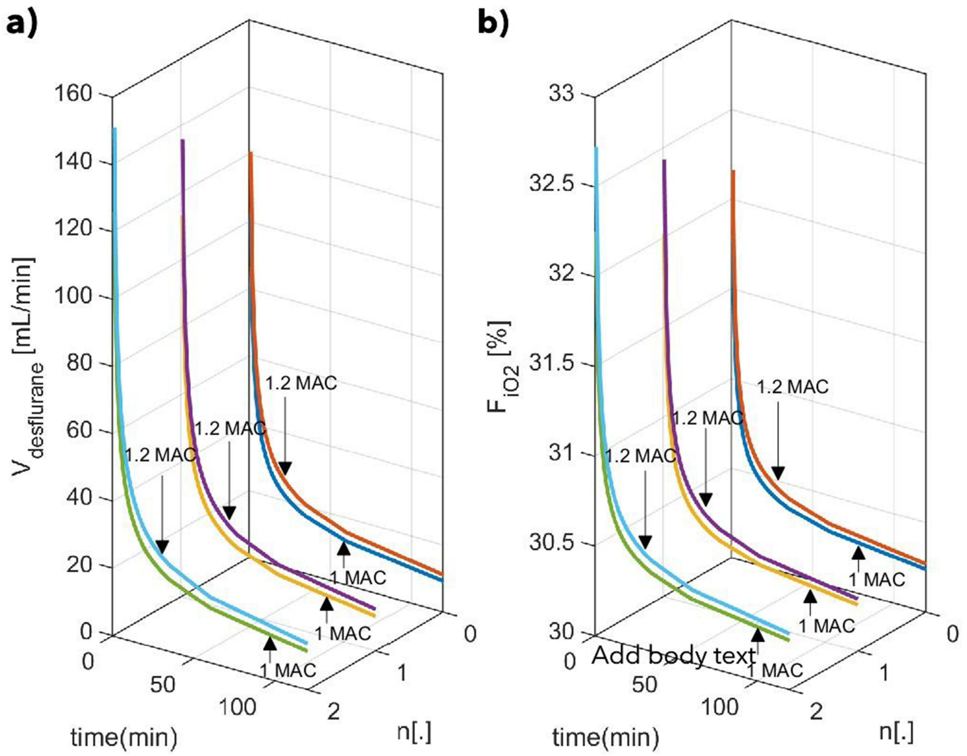

Figure 2 (a) Desflurane uptake, **(b)** concentration of oxygen in breathing gas.

Knowing how parameters change through the impact on the patient, the dynamics of changes in the concentration desflurane on the set input function must be checked. The Figure 3 shows the anesthetic tension of desflurane achieved with combined anesthesia. These results were obtained by using the Gas Man ® program.

This experiment was performed in order to verify the steady-state constant of the $ET_{desflurane}$ concentration of desflurane. The data was determined as $d(VRG_{desflurane})/dt$ and it shows that the highest achievement of the higher concentration is possible by together increasing the fresh gas flow and the concentration in the desflurane vaporizer. The fastest reduction to $1MAC$ is also possible by together reducing the vaporizer concentration with the flow of fresh gases.

Halogenated anesthetic (sevoflurane, desflurane, isoflurane, enflurane, and halothane) decrease mean arterial pressure (*MAP*) with increasing concentrations of the anesthetic gas in a dose-dependent manner.[24]

Mathematical Model of the Desflurane

The given function of increasing the concentration of desflurane can be described by an exponential function. The increase in arterial blood pressure occurs by the operator which damaged tissue. Response of this damage is the neuroendocrine reaction that affects the increase in heart rate (*HR*) and blood pressure. High blood pressure can be decreased by the use of appropriate drugs or by increasing the concentration of desflurane. Desflurane causes the vasodilation of larger arteries influencing this by reducing the blood pressure. The authors of the article defined the limits of expiratory desflurane which do not significantly increase the pressure and flow (*CBF*) and cerebral perfusion pressure (*CPP*). The increase of desflurane function can be described by:

$$Et_{des}(t) = \left(-C_1 e^{\left(-\frac{t-\tau_a}{T1}\right)}\right) \times 1(t-\tau_b) + \left(C_{2(OS)} \times 1(t)\right) \tag{2}$$

where: C_1=2.5 vol/%, *t*-time, T_1=3.965 min, τ_a=14.9808 min, *1(t)*- unit step, $C_{2(OS)}$=7.8 –constant shift in values, τ_b- time constants.

Figure 4 shows the function defined by equation (2). This function represents the beginning of anesthesia, at t = 10 minutes the knob of the desflurane vaporizer is unscrewed. The goal is to achieve a value E_{tdes} at the level 7.8 vol/%. The

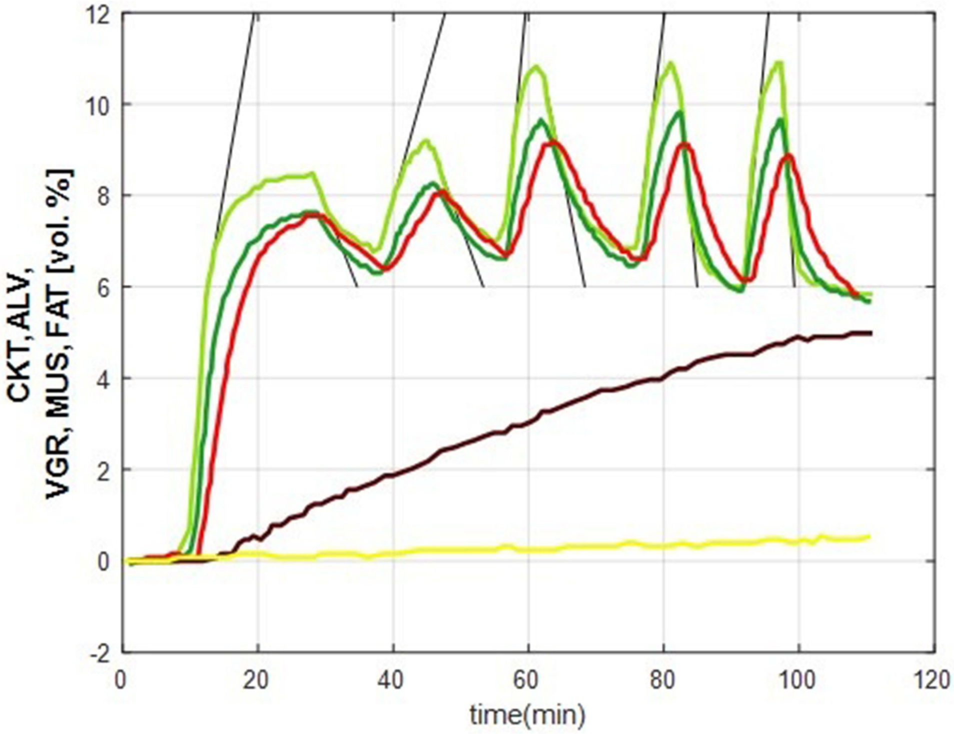

Figure 3 Graphical display of anesthetic administration partial pressure expiratory in response to different inspired concentration of desflurane (*CKT* -circuit, *ALV* -alveolar, *VRG* - vessel-rich- group, *MUS* – muscle (brown line), *FAT* = fat (yellow line)).

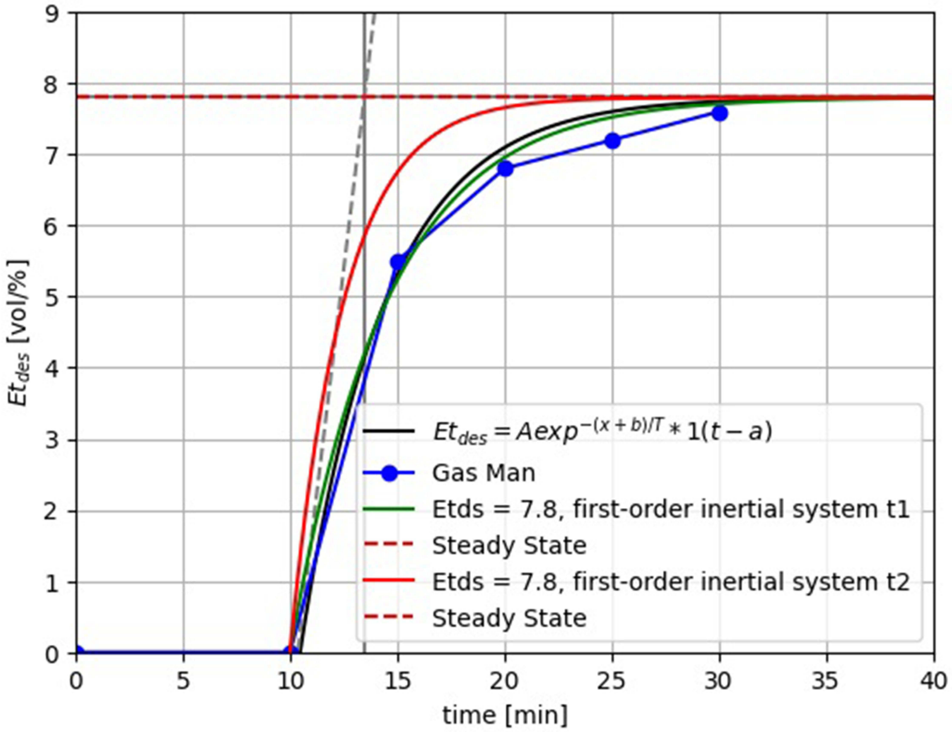

Figure 4 Desflurane concentration (E_{tdes}) waveform generated based on equation (2) and Gas Man software.

function generated using equation (2) is practically consistent with the data obtained from the Gas Man program (see Figure 4 – Gas Man curve), this indicates the advantages of such modeling.

The coefficients on the basis of which the graph (see Figure 4) was obtained by equation (2) are, respectively: C_1=2.5, $C_{2(os)=}$7.8, T_1=3.956, τ_a=14.9808 min and $C_{2(os)}$=7.8 vol/%. These coefficients were selected mathematically. From this function, the time constant can be read. The delay in reaching E_{tdes} can be modeled by the function of a first order inertial term (see Figure 4).

The cardiovascular reaction on increase the desflurane concentration (formula (2)) it can be described by equation (for example, for blood pressure Systolic):

$$P_o(t) = P_1(t) + P_2(t) \tag{3}$$

where: $P_1(t) = \left(P_{1A}e^{\left(-\frac{t+\tau_c}{T_1}\right)} + p_{1(OS)}\right) \times 1(t-\tau_d)$ and $P_2(t) = \left(P_{3(OS)}\right) \times 1(t-\tau_e) \times \left(-1\left(t-\tau_f\right)\right)$

The function (equation (3)) can be presented on a graph Figure 5.

The coefficients on the basis of which the graph (see Figure 5) was obtained for equation (3) are: t-time, P_{1A}=2.52 mmHg, τ_c=−17 min, T_1=4.96, $P_{1(os)}$=137 mmHg, τ_d=12 min, $P_{3(os)}$=144 mmHg, τ_e=0 min, τ_f=12 min, *1(t)* – Unit step.

Impact Fresh Gas Flow on P_{O2} and P_{CO2}

Any technique of the fresh gas flow that is less than the alveolar ventilation can be designated as low-flow anaesthesia. The practicing anaesthesiologists, to move towards the low flow anaesthesia, to achieve lesser environmental pollution and make anaesthesia more economical. The metabolic minute production of carbon dioxide (V_{co}) is approximately 200 mL (0.2 L/min) in a resting adult.[27] The P_{ACO2} (on the assumption P_{ACO2}=P_{Aa}) can be written as a formula:

$$P_{A_{CO_2}} = \frac{V_{co} \times P_I}{V_A} \tag{4}$$

where: V_{co}- metabolic minute production of carbon dioxide, P_I- total pressure at the end of inspiration, V_A- alveolar ventilation.

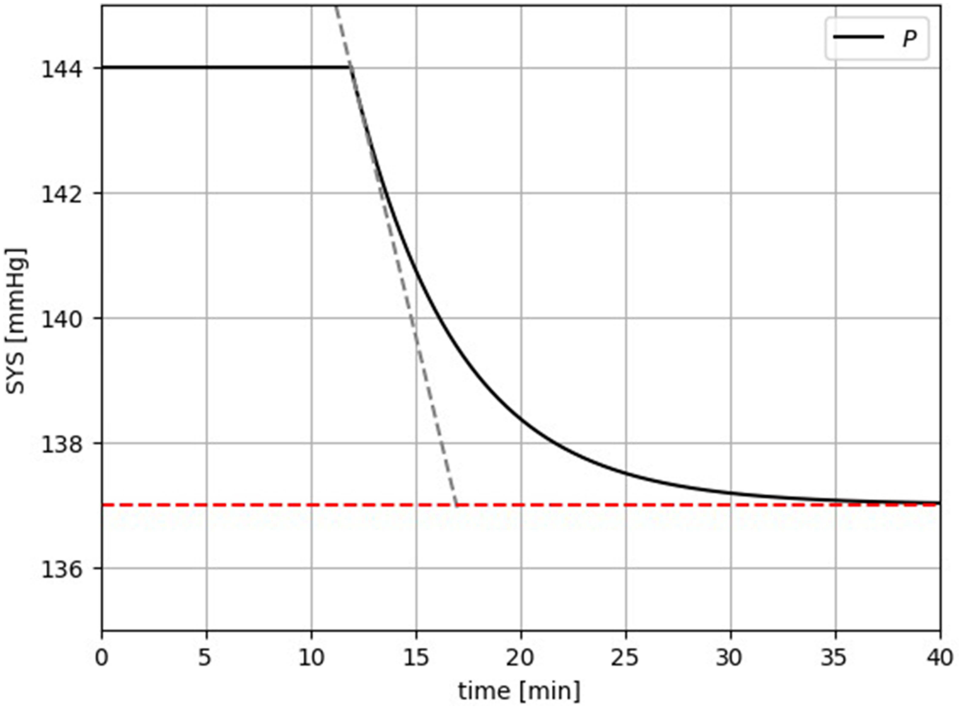

Figure 5 Graphical display a *SYS* blood pressure change over time.

Based on equation (4), the CO_2 (carbon monoxide (IV)) partial pressure increases as the flow of gases delivered to the patient is reduced. The CO_2 pressure has the strongest effect on vasodilation. CO_2 during the expiration phase is one of the most important parameters, which provides valuable information on ventilation efficiency, gas exchange and metabolism. Measurement of CO_2 is taken directly at the end of the endotracheal tube which provides reliable data that is displayed in real time on the ventilator screen.

Body's Reaction to Intraoperative Pain

During the procedure of securing the airway by oral intubation with the use of a laryngoscope, an increase in the patient's arterial pressure and pulse is often observed. This reaction of the patient results from the activation of two systems: the sympathetic-adrenal (*SAM*) and the hypothalamic-pituitary-adrenal (*HPA*) axis, which are controlled by the hypothalamus. Pain stimuli are transmitted through nociceptors made of afferent fibers $A\text{-}\delta$ (myelinated) and C (non-myelinated). Activation of the above system causes the secretion of catecholamines into the bloodstream primarily norepinephrine (*NA*) and adrenaline (*A*), which affect the functions of internal organs. The surgeon's incision of tissues causes an increase in the patient's arterial blood pressure during the conduction phase of anesthesia. These external factors affect the hemodynamics. The value of arterial pressure changes during the operation, therefore there is a need to support the selection of the appropriate value of desflurane concentration at the moment of the procedure in order to avoid the supply of opioid. Halogen anesthetics cause a dose-dependent decrease in arterial blood pressure.

Intelligent System Supporting the Selection of Desflurane Concentration

Due to the many monitors of vital signs working during the procedure, there is a problem in recognizing the meaning of signals, which are additionally dependent on many factors, including pharmacology. Often, the administration of certain drugs causes falsification of the monitored parameter. The system supporting the selection of the appropriate concentration of desflurane is used in clinical practice during the conduction phase of general anesthesia. Data on the pharmacokinetics and pharmacodynamics of this anesthetic were given in the introduction to the article. Because changes in the concentration of desflurane cause changes in the circulatory system, it can be used to stabilize the blood pressure of the anesthetized patient. The mere change of the concentration of the anesthetic in the vaporizer does not affect the quick determination of concentrations in individual compartments of the body. In this situation, the fresh gas flow rate should be further increased to accelerate the achievement of the target (tidal) concentration of desflurane. The proposed concentration control system examines the difference quotient based on adjacent samples of arterial pressure values with a time interval of 5 min. If the quotient value is greater than 5 mmHg, the system is activated. This information allows to determine the moment when the proposed algorithm works most efficiently. When changing the concentration, the algorithm supporting the selection of the desflurane concentration simultaneously monitors the depth of consciousness exclusion using the *BIS* (bispectral index) parameter. Too high a *BIS* signal means a decrease in the loss of consciousness (sedation), while too low a deep sleep (value 40). The control limits of this parameter have been set in the system as an overriding conditional statement.

An algorithm supported by artificial intelligence was used to build a desflurane concentration management system during anesthesia. The main algorithm is the *TSK* (Takagi-Sugeno-Kanga) fuzzy inference system. The fuzzy system works based on the information provided by the expert. The expert connects two input and output spaces using logical sentences written in the form of the *IF-THEN* rule. A set of logical rules is entered into the system database. Rules consist of two parts: premise and conclusion. In the *TSK* reasoning system, in the premise, the input variables are fuzzy, while in the *THEN* part there are functional dependencies. The premise can be composed by using a logical conjunction. The task of the desflurane concentration support system is to generate the optimal E_{tdes} value (end-expiratory concentration value) to maintain stability of the anesthetized patient's hemodynamics. Lowering the arterial pressure resulting from operational stress with desflurane allows to reduce the dose of the used opioid, eg fentanyl. Such a system is possible to implement in clinical practice only for patients qualified for elective procedures and in general health condition assessed as *ASA I* in the state of normovolemia and euthyroidism. The exceptions are procedures involving the removal of the thyroid gland, especially the hyperactive one, due to the possibility of a sudden high release of thyroid hormones affecting the functioning of the cardiovascular system. The problem with the accuracy of the proposed system is also the procedures in which airway protection was performed with a full stomach. Patients for whom assisted anesthesia has been designed, in most cases, their circulatory response to surgical trauma is similar during surgery. The usefulness of assisting in the selection of desflurane concentration applies especially to extensive procedures when it is necessary to use large amounts of opioids. The most important parameters of hemodynamics during planned procedures are systolic (*SYS*) and diastolic (*DIA*) pressure monitored non-invasively by *NIBP* (non-invasive blood pressure) and heart rate (*HR*). The diagram shown in Figure 6 represents the structure of the concentration selection support system. Input data range *DIA* [50,110], *SYS* [90,200], *HR* [40,120], *BIS* [40 60].

Heart rate (*HR*) and bispectral index (*BIS*) values are checked in the main if loop (see Figure 6).

The rule *R* of the anesthesia support system will be written in the form of $R^{(1)}$: *IF* (*DIA* is $A_1^{(1)}$) *AND* (*SYS is* $A_2^{(2)}$), *THEN* (E_{tdes} *is* y_1), where: *AND*- logical connective, *A*-fuzzy set determined by the membership function, y_1-functional dependence representing the desired value of E_{tdes}. Since the system built in this way causes the problem of multi-dimensionality, the authors of the work minimized it by limiting it to only two input variables *DIA* and *SYS*. The *HR* and *BIS* values are checked in the if conditional statement and depending on its value, a given subsystem is started. The antecedent sets of the $R^{(1)}$ rule are defined by the Gaussian membership function (Figure 7 – *inputmf* network layer) for each input variable *DIA* and *SYS* with the relation:[28]

$$\mu_A(x) = \frac{1}{1 + \left(\frac{x-c}{\sigma}\right)^{2b}} \tag{5}$$

where: *x*–input variable *DIA* or *SYS, b*-shape of the Gaussian membership function μ, *c*- location of the center of the Gaussian membership function μ, σ- width of the Gaussian membership function μ.

The proposed system works in an open *MISO* system (multi-input multi-output). The input of the subsystem (Figure 7 - input) is defined by the vector *in*=[*DIA SYS*]^T, where: *T* – is the transposition operator of the input vector in.

The *TSK* fuzzy controller shown in Figure 7 generates an output value (Figure 7 - output) based on the dependencies:[28]

$$y(\boldsymbol{in}) = \frac{\sum_{k=1}^{M}\left[\prod_{j=1}^{N}\mu_A^{(k)}\left(in_j\right)\right]\left[y_{k0}\right]}{\sum_{k=1}^{M}\left[\prod_{j=1}^{N}\mu_A^{(k)}\left(in_j\right)\right]} \tag{6}$$

where: in_j – *j*-th variable of the input vector *in*, Gaussian membership function μ defined by relation (5), y_{co}-sharp dependence in the successor of the fuzzy rule *R* representing E_{tdes}, *Π*- algebraic product of fuzzy sets.

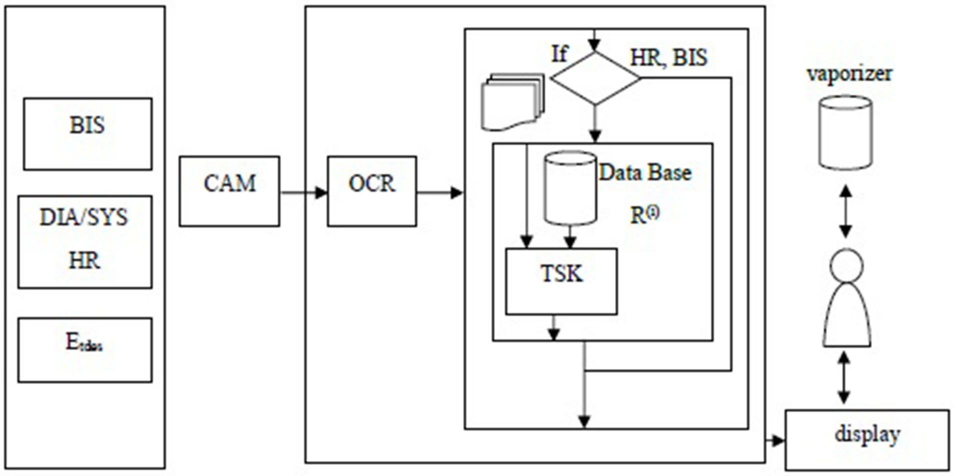

Figure 6 Graphical display the system of supporting the selection of desflurane concentration (where: *OCR*- optical character recognition, *CAM*- camera).

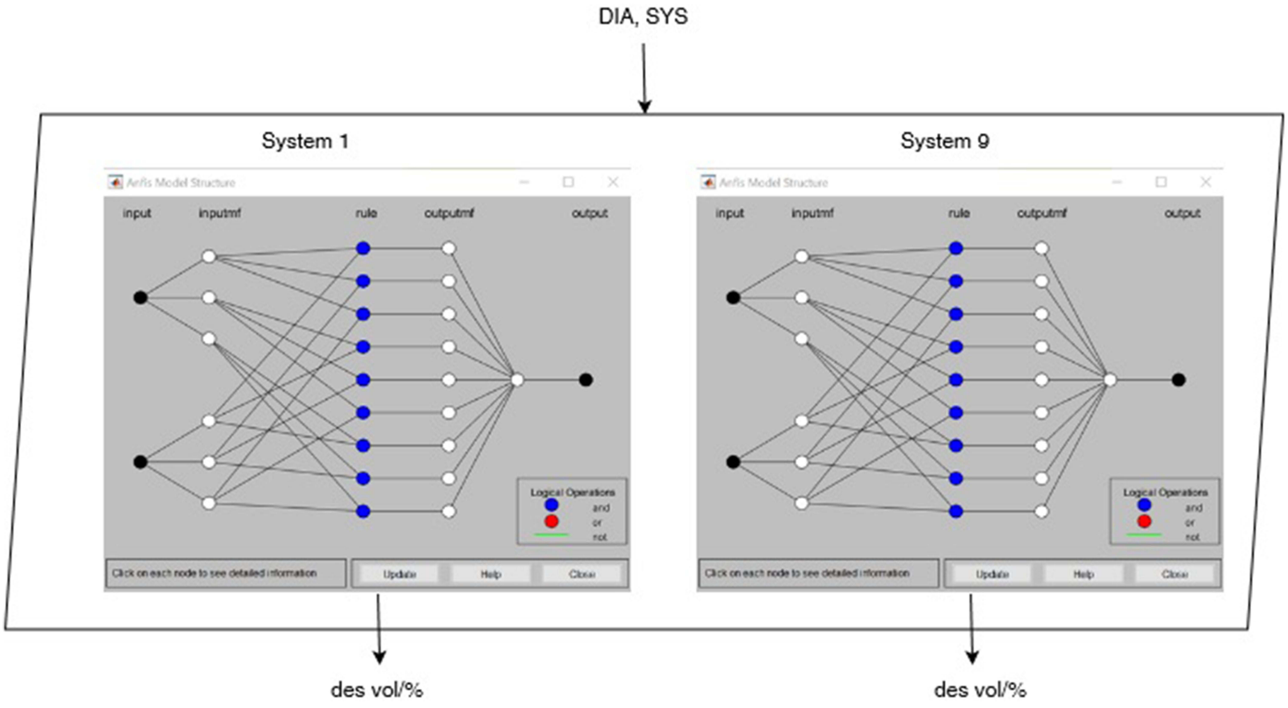

Figure 7 Diagram of anesthesia support controller.

The parameter defined by the relationship (6) represents the desired value of E_{tdes}, which reduces the circulatory pressure to the input value (physiological blood pressure of the anesthetized patient). A detailed description of the principle of operation of the neuro-fuzzy controller based on *TSK*-type reasoning is presented in these studies.[28–30]

The input/output variable range of each of the nine subsystems varies from minimum to maximum for: *DIA* [50,110], *SYS* [90,200], *HR* [40,120], *BIS* [40 60]. The number of membership functions for each input variable *DIA* and *SYS* is 3. The proposed system automatically generates rules on the basis of data provided in the training set. For example, Table 1 shows the training set for the first subsystem. This system is built on the basis of the *SYS* and *DIA* input values and the E_{tdes} output value, while it is run by the superior instruction "if".

Table 1 contains the possibilities of changing blood pressure during tachycardia of an anesthetized patient. The data in Table 1 can be described by an algorithm based on if or otherwise conditional statements. This type of control determines the hard bounds of a set by assigning elements to it with must (1) or not belong (0). Since it is difficult to define all

Table 1 Input Signals of the Desflurane Subsystem Generating Concentration Based on the Arterial Circulation Parameters of the Anaesthetized Patient

SYS [mmHg]	*DIA* [mmHg]	*HR* [min^{-1}]	BIS	Et$_{des}$ [Vol/%]
90	50	120	40–60	6
100	60	120	40–60	6
120	80	120	40–60	6.6
140	90	120	40–60	6.6
150	95	120	40–60	7.8
170	100	120	40–60	7.8
200	110	120	40–60	7.8

possibilities with a minimum step of the difference between successive blood pressure values (eg by 5 mmHg), an intelligent algorithm in the form of a neural fuzzy network was used for this purpose. It allows fuzzy determination of transition limits between the next change defined in the training set of the neural fuzzy network.

The entire desflurane concentration selection system consists of nine subsystems based on appropriate tabularized training sets. On the basis of dependence (6) and input data ranges, as well as the adopted number of learning epochs of the neural fuzzy network, which is 250 (learning step), surfaces representing the operation of individual subsystems of the proposed system were generated. Figure 8 shows the surfaces representing the operation of the first subsystem based on the learning data given in Table 1.

The relevant points of the input space determined by the relation (6) are shown in Figure 8. The other subsystems differ only in the ranges of variables in relation to the hypersurface shown in Figure 8. Training data containing two columns-input vector (*DIA* and *SYS*) and output value (E_{tdes}). The baseline value (E_{tdes}) takes the number that should lower the patient's blood pressure and illustrates the appropriate case (eg Table 1, line 1 means the case: Low blood pressure with tachycardia and anesthesia sleep deep enough, leave the vaporizer setting to *1MAC*). Any value measured by the *NIBP* device that differs from the physiological values of the anesthetized patient triggers the algorithm and, in addition to setting the end-expiratory value of E_{tdes}, it is required to set the appropriate *FGF* fresh gas flow. The analysis of the impact on achieving a rapid concentration of desflurane in a given compartment is presented in Figure 3. Some cases of the anesthetized patient's health condition require other coordination than changing the concentration of gases such as opioid supply.

The article presents an algorithm that allows deducing, on the basis of neighboring sets, the response to an input (*DIA, SYS*) that does not have a value that is the center of a given set. This task can be accomplished with fuzzy algorithms. The plane of the controller's operation can be represented in a system with two inputs described by a function connecting the centers of the input sets by means of a polynomial. This approach indicates problem solving by means of a non-mathematical description of control systems using linguistic control using the rules *IF - THEN* (condition/conclusion). Thanks to the rule base, the system can be expanded by adding expert information. Such evolution of the system allows to increase the accuracy of control by the users of this system. This possibility is very important because each patient may react differently to nociceptive stimuli and anesthetic drugs. There are no universal systems that can solve the problems of inhalation anesthesiology. Therefore, the table is a form of approximation of a given case. The proposed

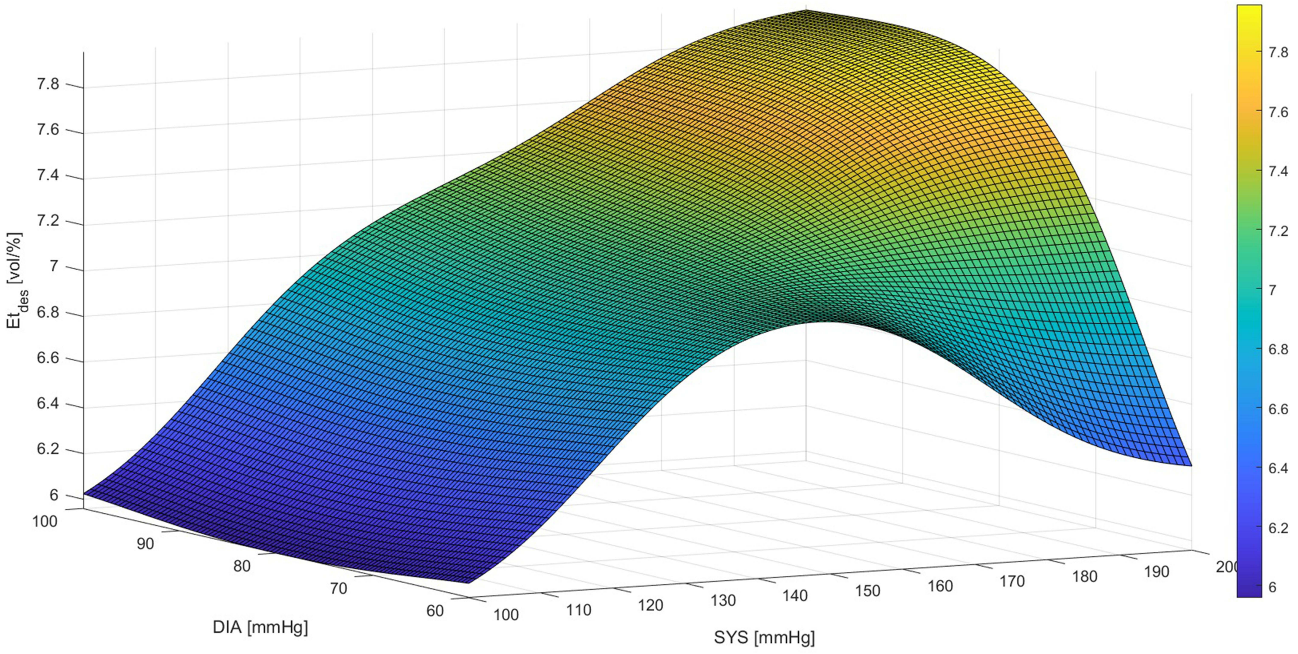

Figure 8 Hypersurface representing the operation of the desflurane concentration selection subsystem controller based on the data inTable 1.

system has safety limits consisting in determining the conditions of desflurane concentration values and flows. Each input variable *DIA, SYS* is defined by three fuzzy sets. Assignment of a given input element to a set is performed using the membership function. Due to the easy description of the Gaussian membership function, it was chosen for the proposed system. The neural network system, on the basis of the teaching and testing data, sets appropriately the vertices of the membership functions in individual input spaces of the control system of a given subsystem. The Matlab program with the Fuzzy Logic program was used to learn the network. After the study, the distribution of the membership function presented in Figure 9 was obtained.

Figure 9 for the subsystem related to tachycardia with the possibilities of changing the circulation given in Table 1 shows the distribution of Gaussian functions in the input space of the controller. Functions set in this way allow to generate the surface shown in Figure 8. This surface allows for continuous control of the selection of desflurane concentration even between the defined grid points specified in Table 1.

The article analyzes the influence of the *FGF* fresh gas flux value in order to quickly achieve the concentration of desflurane in *VRG* tissues rich in blood. The higher the flow, the greater the ramp-up constant of the desflurane concentration in the *VRG*. Therefore, in order to achieve a quick effect of reducing circulation, it is necessary to increase the flow of *FGF* gases to a value not exceeding 6 L/min together with increasing the value on the desflurane vaporizer to 12 vol./%.

Results

The proposed concentration selection algorithm can be used after induction of anesthesia, as shown in the graph in Figure 6. The input data in Table 2 was used to verify the correct operation of the desflurane concentration selection algorithm. The 1 *MAC* value was determined based on the Mapleson $MAC\ (40yo)\times 10^{(-0.00269\times(AGE-40))}$.

The values contained in the last column of Table 2, containing the parameter of expiratory concentration E_{tdes}, are generated from the concentration selection algorithm based on the *SYS* and *DIA* input values (columns 1 and 2 in Table 2). The E_{tdes} values affect the BIS index parameter, and if it drops below 40, the algorithm proposes to quickly reduce E_{tdes} to the value

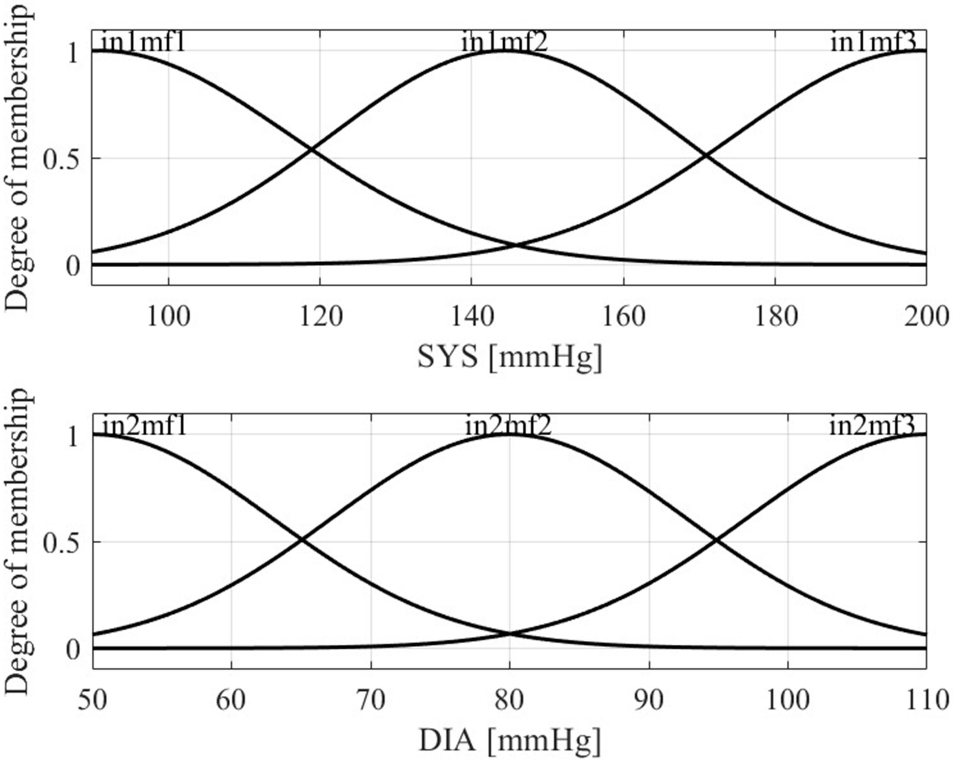

Figure 9 Membership functions for *SYS* and *DIA* parameters.

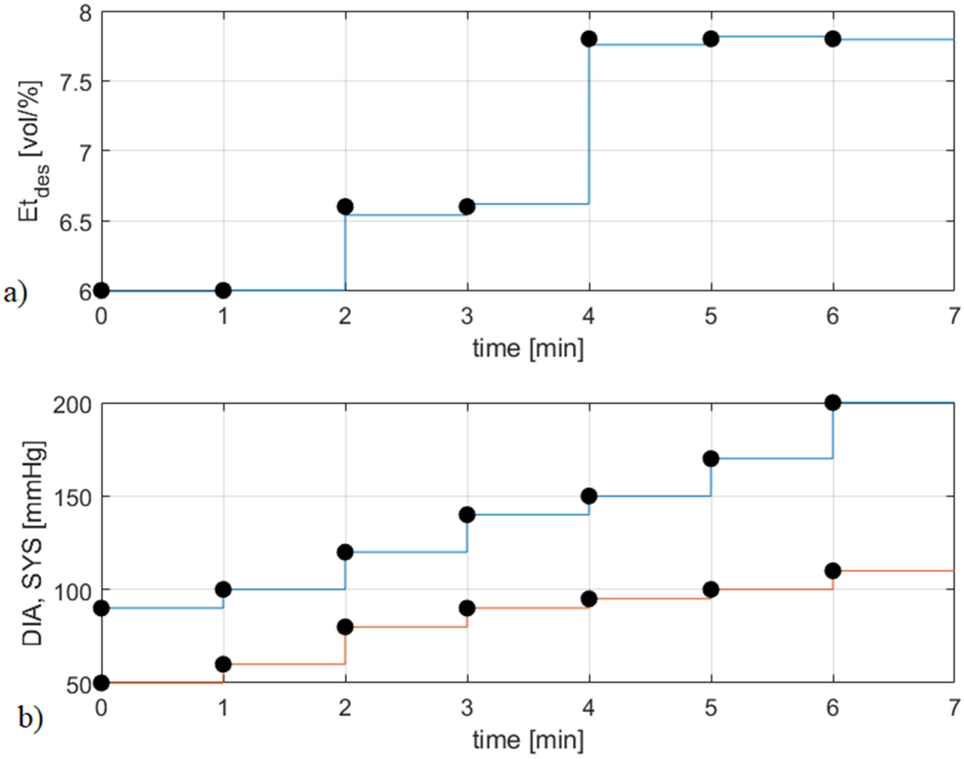

Figure 10 Waveforms: (**a**) output of the algorithm - Etdes and (**b**) input DIA/SYS.

of 1*MAC*. In order to quickly achieve the effect of lowering the arterial pressure of the anesthetized patient, the supply of fresh gases to the respiratory system is increased to the value corresponding to minute ventilation of 6 L/min. Based on the heart rate value, one of the 9 subsystems is activated. Since in the *HR* value is variable, the individual subsystems will be activated accordingly. The advantage of the proposed algorithm is the generation of the required E_{tdes} value, which has not been defined by an expert in the training set (example set - Table 1). This problem requires a proper definition of the solution search space points. For another example of the patient's changing arterial circulation (Figure 10b) during anesthesia, the algorithm generated the end-expiratory E_{tdes} values (Figure 10 a) which should bring them down to the physiological value.

Since the algorithm is designed for healthy patients, the blood pressure value is defined as 120/70 mmHg.

The values obtained in the graphs were generated by the Matlab computer program. The input points of the *DIA* and *SYS* algorithms are shown in Figure 10b, while the output is the desired value of the end-expiration of desflurane. This value should allow the pressure to drop to the physiologically correct value.

Table 2 Desflurane Concentration Selection Algorithm Test Data

Sys [mmHg]	*Dia* [mmHg]	*Hr* [min^{-1}]	*BIS*	Et_{des} [vol/%]
120	70	70	50	6
140	80	75	50	6.2
140	85	100	50	7.2
150	90	100	50	7.7
160	90	90	50	7.8
170	90	100	50	7.8
200	100	100	50	7.8

There is a difference between the values marked on the evaporator and E_{tdes}. The algorithm works on the principle of unscrewing the evaporator to a value 2 times greater (values on the evaporator scale) than 1 *MAC* determined from the exhaust gas parameter and increasing the *FGF* to about 6L/min. Using the algorithm, the E_{tdes} signal should be monitored, and if the value determined by the algorithm is reached, the evaporator should be turned to the value ensuring 1 *MAC* in about 5 minutes with gas reduction to 2 L/min.

The proposed algorithm has applicability in the anesthetic system. It can be used as a digital support during anesthesia as a mobile application. Ease of use consists only of entering input data measured with a time interval of 5 minutes. The pressure values data are needed for the anesthesia report so archiving them is necessary. The proposed algorithm can introduce them from the report into the calculations and generate the values that should be set to lower the patient's pressure. Reducing the leaves of opioids improves anesthesia conditions and reduces the possibility of hyperalgesia.

Discussion

The proposed system based on *AI* (Artificial Intelligence) allows for an innovative way to model the complex mathematical problem of selecting the concentration of anesthetic gases (desflurane). The problem related to the supply of opioids is known, and the solution may be to try to control the body's circulatory response to surgical pain.

Dexter et al[31] discusses the termination of anesthesia based on sevoflurane. An important point of this article is to achieve a change in the expiratory concentration of sevoflurane without shutting down the evaporator with or without changing fresh gas flows. The authors emphasize the reliability of "smart" machines that are focused on performing their intended purpose. Dexter et al[31] is an important contribution to the development of the authors' work due to the analysis of the impact of anesthetics on the environment. Due to the impact of desflurane on the environment, the authors of this article recommend, based on simulations in the Gas Man program, to increase the *FGF* flow to no more than 8 L/min in order to achieve the set concentration. For the case of the anesthesia time interval: *FGF* = 2 L/min for 5 min (desflurane: 6 vol/%) with a change to 8 L/min (desflurane: 8 vol/%), the carbon dioxide equivalent value CO_2e = 70 kg will be obtained for comparison with sevoflurane, the carbon dioxide equivalent for the same regimen is 1.4 kg. With higher flow, this parameter increases. Despite the large environmental impact of desflurane, reducing the supply of opioids is now more important.

The obtained results prove the effectiveness of the use of intelligent systems that easily model complex medical processes without knowledge of the mathematical description. The authors' research plans related to the development of two phases of supporting and waking up the patient.

Conclusion

Mathematical analysis of the body's reaction to the set inspiratory value of desflurane allowed for the design of a function that reproduces this process. The authors decided to provide simple exponential functions and parameterize them in such a way as to model the process without the use of approximation using high-order polynomials. This approach allows you to easily model the entire process presented in the graph in Figure 6.

Author Contributions

BD wrote the manuscript, AC and BR analysed algorithm, CK helped collecting data in medical simulation center, PR and TG reviewed and corrected manuscript. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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