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Advanced lung ventilation system (ALVS) with linear respiratory mechanics assumption for waveform optimization of dual-controlled ventilation

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Abstract

The present paper describes the functional features of an advanced lung ventilation system (ALVS) properly designed for the optimization of conventional dual-controlled ventilation (DCV), i.e. with pressure-controlled ventilation with ensured tidal or minute volume. Considering the particular clinical conditions of patients treated with controlled ventilation the analysis and synthesis of ALVS control have been performed assuming a linear respiratory mechanics. Moreover, new airways pressure waveforms with more physiological shape can be tested on simulators of respiratory system in order to evaluate their clinical application. This is obtained through the implementation of a compensation procedure making the desired airways pressure waveform independent on patient airways resistance and lung compliance variations along with a complete real-time monitoring of respiratory system parameters leading the ventilator setting. The experimental results obtained with a lung simulator agree with the theoretical ones and show that ALVS performance is useful for the research activity aiming at the improvement of both diagnostic evaluation and therapeutic outcome relative to mechanical ventilation treatments.

Keywords: Mechanical ventilation; Dual-controlled ventilator; Tidal volume; Minute volume; Waveform optimization; Real-time respiratory mechanics evaluation; Respiratory mechanics linear model

1. Introduction

As it is well known, artificial lung ventilation plays a fundamental role in several health critical applications, with main clinical indications in anaesthesia, particularly during long lasting operations, in Intensive Care Units and in the respiratory insufficient syndrome [1].

Thus, since the introduction of artificial respiration in the clinical practice, the design and the functional features of lung ventilators have been undergone a continuous evolution and improvement till today [2,3]. The recent developments of ventilators technology have provided electro-mechanical devices able to perform the automatic control of artificial ventilation through a microprocessor feedback acting between preset and actual measured values of basic physical parameters [4–6]. Nevertheless, the crucial still unsolved question is the optimal choice of ventilation modality and parameter setting to be applied to the specific patient and pathology [7,8].

Nowadays most clinicians select the technique and parameter settings to be adopted for the ventilation treatment among the conventional modalities included in the own ventilator options without taking advantages of real state of the art. The existing gap between the technology outcomes currently available on ventilators and their implementation in the clinical practice comes from different historical and cultural reasons [9].

Firstly, it should be pointed out the lack of a scientific communication channel connecting effectively the clinical environment with the physical and engineering fields. Moreover, the clinical training and experience of medical staff

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usually does not provide an adequate knowledge of physics as well as of technology involved in the mechanics of lung ventilation. Such widespread situation brings about three substantial main drawbacks. The first drawback consists in the strong slowing down of research and development activity applied to the field. The second drawback is the lack of consensus working protocol between different personnel involved in testing and evaluating both the clinical results and the adopted research approach. The last, but of course most relevant drawback, is the negative effect on the patients which otherwise could take advantages of the improved and advanced procedures applied to the clinical practice.

In order to overcome such problems, a new idea should be found out. This purpose can be reached through a strong effort towards a multidisciplinary approach based on a close joining of competence activity between biophysicists, bioengineering and clinical physicians. This cooperation may also lead to the design guidelines for optimal and advanced ventilators as well as to their laboratory and clinical developing and testing.

The present paper deals with the design description and functional features of an advanced lung-ventilator system (ALVS) conceived for analysis and control of improved artificial ventilation modalities. Besides that, properly developed procedures for the optimization of respiratory flow, airways and endoalveolar pressure waveforms during assisted/controlled ventilation, useful in the research and clinical activity, will be defined and discussed.

2. State of the art and research requirements for assisted/controlled ventilation

Controlled ventilation should be applied to the patient when his spontaneous breathing is absent or forbidden for the whole duration of the treatment. Controlled ventilation includes all that ventilation modalities in which the breathing control is completely carried out by an external machine, i.e. the ventilator [10].

When spontaneous breathing is present, even if below the standard physiological level, assisted/controlled ventilation is required for the patient. Assisted/controlled ventilation is so called because it includes all the ventilation modalities in which the ventilator supplies the patient with controlled breathing only after a long lasting interval of apnea (assisted ventilation) or at detection of a very weak effort of spontaneous breathing (triggered ventilation) [11]. Thus, in assisted/controlled ventilation the control of breathing is partially held by the ventilator, anyway allowing the patient the possibility of spontaneous breathing at his will or capability [10,11].

The controlled breathings supplied to the patient during controlled or assisted/controlled ventilation can be classified considering different approaches [10]. The most practical and consequently most diffused approach is based on the physical parameters controlled during the inspiration by the pneumatic generator irrespective of load (respiratory characteristics of patient) variations or fluctuations [12].

If during the inspiration the generator supplies the load (lungs) with a pre-established volume (tidal volume) or applies a pre-established pressure to the load (airways), the controlled breathing is defined as volume-controlled ventilation (VCV) or pressure-controlled ventilation (PCV), respectively [12].

In current ventilators used in the clinical practice for controlled breathing of patient, the VCV or the PCV are mainly implemented with constant inspiratory flow or airways pressure, respectively [13]. Such strong limitation in waveform modeling of physical parameter controlled by the ventilator, resulting from simplified hardware and software design, reduces drastically the functional versatility of the ventilator performances.

As a result, among the wide variety of inspiratory waveforms potentially applicable to the patient treated with assisted/controlled ventilation, the square shape is the only option practically employed in the clinical environment. The square shape results since at the end of inspiration time in the VCV or in the PCV the flow is abruptly reversed (Fig. 1a) or the airways pressure is abruptly reduced to its lowest value required and preselected for the end of expiration time (Fig. 1b), respectively. Thus, for the controlled breathing of patient the current choice is only between conventional VCV and PCV, i.e. between respiratory flow and airways pressure square waveform, respectively [13].

Until few years ago the VCV has been mainly adopted, with the exception of neonatology field where the PCV is

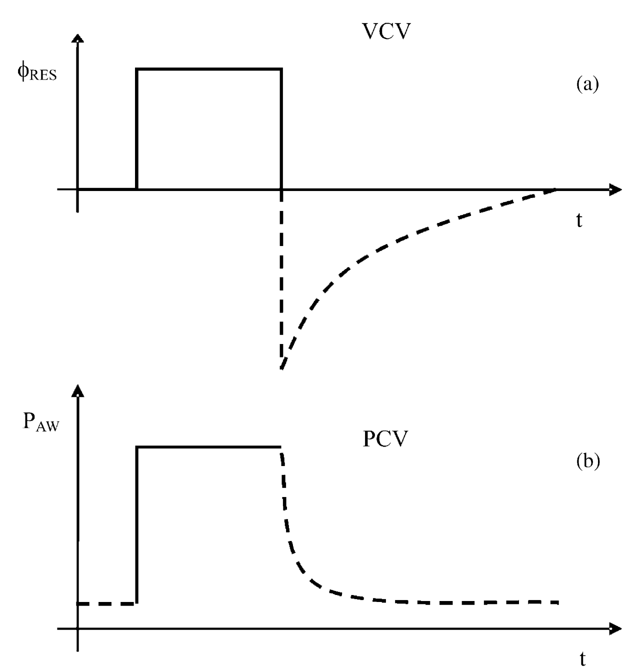

Fig. 1. (a) Square waveform of respiratory flow (ϕ_{RES}) and (b) airways pressure (P_{AW}) as a function of time (t) in conventional volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV). The continuous and dotted lines denote inspiration and expiration, respectively.

preferred since tidal volume control is too much critical [14]. Such situation has been correlated with the clinical assumption that considers the control of tidal volume or of minute volume (volume delivered in a minute) as the most relevant parameter for adult ventilation treatment [13]. This assumption does not take into account the lower physiological character of VCV as well as the high level of intrinsic risk for the patient or functional failure of tidal volume computation.

As it is well established, the mechanics of physiologic breathing is controlled by impressing the proper time variations of transpulmonary pressure for producing the required time variations of respiratory flow and hence of lung volume (and not vice versa) as a function of current value assumed by patient's airways resistance and lung compliance [15]. The transpulmonary pressure is the difference of pressure existing between airways and intrathoracic levels.

Moreover, over long periods of treatment with VCV an overestimated tidal volume can cause the rupture of pulmonary alveoli (risk of "volutrauma"), in particular for reduced lung compliance, whereas an insufficient tidal volume can lead to hypoxia [13].

Finally, the VCV has no capability in providing for pneumatic losses that might occur along the ventilation circuit due to tidal volume measurement at upstream level.

Considering the previous drawbacks, the PCV should be preferable even if the method of measuring and controlling the pressure at the airways level, while eliminating the risk of rupturing the alveoli ("barotrauma"), can easily lead to hypoxia for reduced tidal volume due to the frequent formation of catarrh in the patient's upper airways or in patients having high airways resistance (acute bronchial asthma attack, bronchial spasms, etc.) [12]. In such case, during the inspiration time, the constant value of pressure set for airways pressure is quickly reached, due to the considerable dynamic drop in pressure which occurs between the patient's airways and alveoli, without, however, guaranteeing the patient a sufficient degree of ventilation [12].

The solution of the best choice between current available conventional waveforms for assisted/controlled ventilation consists in the implementation of the so-called dual-controlled ventilation (DCV), i.e. the pressure-controlled ventilation with ensured tidal or minute volume [16,17].

The conventional DCV is a special form of PCV in which the constant level of inspiratory airways pressure is not kept on the pre-selected value but it is automatically regulated by feedback control for delivering during the selected inspiration time either the tidal volume required or, considering the breathing frequency selected, the minute volume pre-established [18].

Is the conventional DCV the final solution for waveform optimization in assisted/controlled ventilation? Not yet.

Two functional improvements should be pursued to the purpose. The first improvement consists in a different advanced approach for the breathing control of DCV with square waveform as airways pressure excitation. Instead of arbitrary pre-established parameters, the ventilation control takes into account the current respiratory characteristics of patient and his diagnostic evaluations, both obtained from a monitoring system [19,20]. The second improvement consists in a more realistic approximation of the airways pressure waveform to physiological transpulmonary pressure waveform. The optimization of such excitation waveform for patient (airways pressure waveform) would allow to reach a more physiological reaction waveform of patient (respiratory flow and endoalveolar pressure waveforms). Moreover, such reaction fits better the current value assumed by patient's airways resistance and lung compliance as well as its physiopathological fluctuation during the treatment [21].

In this regard, the smoothing of upward and downward slopes at the beginning and at the end of inspiration is the most relevant change to be applied on square airways pressure waveform. It allows, indeed, the elimination of the respiratory flow vertical transitions occurring at the beginning of both inspiration and expiration.

The present work deals with the design requirements implemented in the ALVS for performing both the abovementioned functional improvements along with the theoretical treatment and experimental tests relative to the first one. Moreover, the performance of a compensation procedure developed to let the selected airways pressure waveform become stable and insensitive from the patient's breathing characteristics, will be discussed.

3. The design of the advanced lung ventilation system (ALVS) for waveform optimization of DCV

The chance of an improved DCV available in the clinical practice has been enough explained in Section 2. In such context, "improved" means as far as possible similar to physiological breathing pattern together with extremely flexible in adapting to individual patients' requirements, pathologies and their evolution.

The lung-ventilator system (LVS) is the result of the coupling between a breathing machine (lung ventilator) and human lungs [22,23]. The interaction of a ventilator device (generator) with the respiratory system of a human being (load) treated with assisted/controlled ventilation, can be effectively studied adopting a proper fluidodynamic model. The characterization of such model should be carried out taking into account the behavior of every component making up the LVS along with their pneumatic coupling during the breathing process.

As a result, the model should be well suited for studying the steady states as well as the transient evolution assumed by the LVS during the ventilation process [24]. The ALVS has been conceived and developed in our research laboratory in order to perform the waveform optimization of DCV parameters (airways and endoalveolar pressure, respiratory flow and lung volume).

The ALVS main functional units, shown in the Fig. 2 together with their physical connection, are represented by

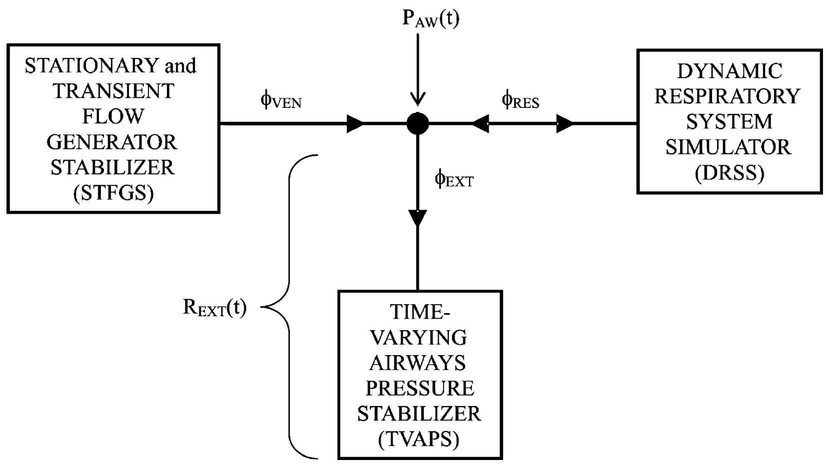

Fig. 2. The advanced lung-ventilator system (ALVS). The STFGS, TVAPS and DRSS units are pointed out along with significant ventilation parameters considered in the text (ϕ_{VEN}; ϕ_{EXT}; ϕ_{RES}; $P_{AW}(t)$; $R_{EXT}(t)$).

the implementation of the following three devices:

(1) stationary and transient flow generator stabilizer (STFGS);
(2) time-varying airways pressure stabilizer (TVAPS);
(3) dynamic respiratory system simulator (DRSS).

The ALVS design has been carried out in order to put into practice the DCV including the following functional performances:

(1) capability of applying to the patient's airways any pressure waveform of clinical interest during both the inspiration and the expiration time;
(2) insensitivity of such waveform in shape and intensity to the load (respiratory parameters of patient) fluctuations or variations;
(3) capability of monitoring pressure waveform (airways and endoalveolar), respiratory flow and lung volume as a function of time together with the lung volume-airways (endoalveolar) pressure and respiratory flow-lung volume loops, as well as power of calculating the current value of inspiratory and expiratory airways resistance, static and dynamic lung compliance and respiratory work;
(4) compatibility of spontaneous breathing activity of patient by flow or pressure support ventilation with assisted/controlled breathing or/and triggered ventilation.

As it is clear from Fig. 2, the points (1) and (2), i.e. the application of the pre-established airways pressure waveform ($P_{AW}(t)$) and its keeping irrespective of the current value assumed by any other pre-set parameter as well as of load (airways resistance and lung compliance) fluctuations or variations, can be achieved by means of a steady flow (ϕ_{EXT}) crossing a time-varying fluidodynamic resistance ($R_{EXT}(t)$). Regulation and control of the steady flow and of the fluidodynamic resistance are implemented inside the STFGS and the TVAPS, respectively.

The Fig. 3 shows the coupling between the STFGS, the TVAPS and the DRSS and their internal configurations including the monitoring system and two on–off flow switches (S1 and S2). The monitoring system, required to fulfill the above-mentioned point (3), consists of two transducers for forward or ventilation (ϕ_{VEN}) and backward or external (ϕ_{EXT}) flow measurement together with two transducers for airways (P_{AW}) and endoalveolar (P_{EA}) pressure measurement.

The STFGS consists of the series between a variable pressure generator (P_G) and its time-varying resistance (R_G).

The TVAPS implements a time-varying resistance ($R_{EXT}(t)$) placed between airways and ground (atmospheric) level.

The DRSS includes a variable resistance (R_P) connected in series with a variable elastic compliance (C_P) simulating, respectively, the airways resistance and the lung compliance of a wide variety of patients and pathologies. The adopted simulator device is extremely simple, but it is adequate for treating all patients' cases with homogeneous respiratory features (see Section 5).

The STFGS has been specially designed for independent stabilization of the flow crossing the TVAPS (ϕ_{EXT}) both in stationary and in transient conditions. Stationary and transient conditions occur when the respiratory flow (ϕ_{RES}), i.e. the flow crossing R_P, equal to the difference between ϕ_{VEN} and ϕ_{EXT} is zero or not, respectively, on account of zero or non-zero difference between P_{AW} and P_{EA} pressure, respectively.

During stationary conditions the STFGS delivers to the TVAPS the steady flow ($\phi_{EXT0} = \phi_{VEN0}$) required for the control and the stabilization of pre-established positive end expiratory airways pressure ($PEEP_{EXT}$) on account of each previous monitored expiration. ϕ_{VEN} control and $PEEP_{EXT}$ control and stabilization irrespective of load fluctuations or variations are actually carried out through the regulation of P_G and equilibrium R_G (R_{G0}) values along with lowest available R_{EXT} value (R_{EXT0}), if both the following conditions are

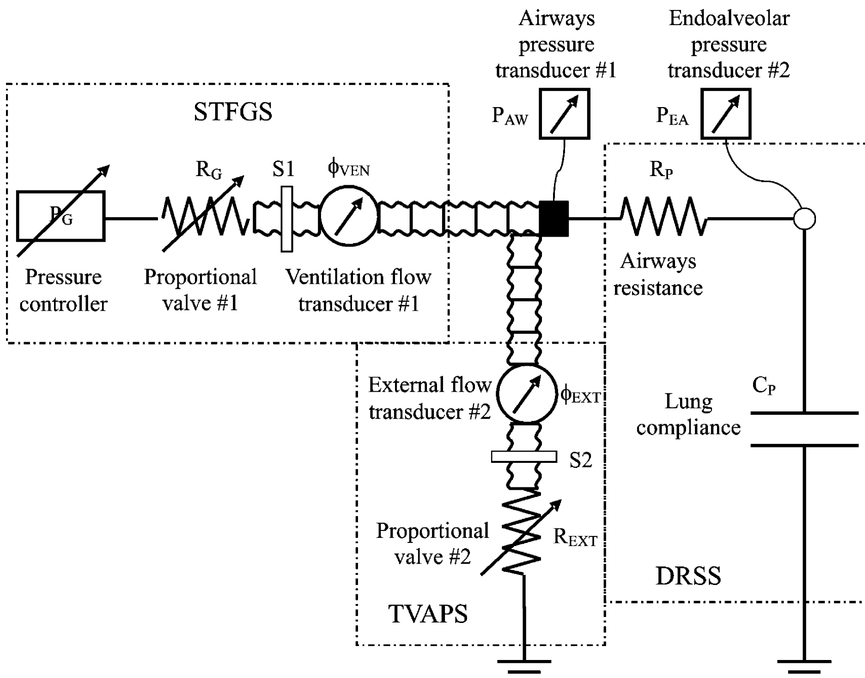

Fig. 3. Internal configuration of the STFGS, TVAPS and DRSS units including the monitoring system of the ALVS. The components crossed with folded arrows are devices whose characteristic parameter output can be varied according to input setting control.

verified:

$$R_{G0} \gg R_{EXT0} \tag{1}$$

$$P_G \gg \mathrm{PEEP}_{EXT} \tag{2}$$

The conditions (1) and (2) establish that the value of R_{G0} and P_G should be considerably greater than R_{EXT0} and selected PEEP_{EXT} values, respectively.

Considering both the conditions (1) and (2), the following relations apply for independent control of ϕ_{VEN} and PEEP_{EXT}:

$$\phi_{EXT0} = \phi_{VEN0} = \frac{P_G}{R_{G0}} \tag{3}$$

$$\mathrm{PEEP}_{EXT} = R_{EXT0}\phi_{EXT0} = \frac{P_G}{R_{G0}} R_{EXT0} \tag{4}$$

Therefore, considering that R_{EXT0} is a fixed parameter, the control of both the desired ϕ_{VEN} and the selected PEEP_{EXT} values is performed via P_G and R_{G0} regulation under both conditions (1) and (2).

The transient conditions are correlated to the presence of non-zero ϕ_{RES} during both inspiration (ϕ_{INS}) and expiration (ϕ_{EXP}), occurring when P_{AW} is increased from PEEP_{EXT} up to its maximum value (P_{GI}) and soon after decreased down to the same PEEP_{EXT} value, respectively.

The desired $P_{AW}(t)$ is obtained during inspiration and expiration by R_{EXT} increasing from R_{EXT0} up to its maximum value (R^*_{EXT}) and soon after decreasing down to the same R_{EXT0} value, respectively.

For the same reasons described above in the stationary case, both the following conditions should be verified:

$$R_{G0} \gg R^*_{EXT} \tag{5}$$

$$P_G \gg P_{GI} \tag{6}$$

Considering that R^*_{EXT} and P_{GI} values are obviously greater than R_{EXT0} and PEEP_{EXT} values, respectively, both the conditions (1) and (2) can be neglected.

According to both the conditions (5) and (6) the following relation applies for P_{GI} control:

$$P_{GI} = R^*_{EXT}\phi_{EXT0} = \frac{P_G}{R_{G0}} R^*_{EXT} \tag{7}$$

During both inspiration and expiration the presence of non-zero ϕ_{RES}, if not compensated, would bring about a fluctuation of ϕ_{EXT} around ϕ_{EXT0} value and in turn a $P_{AW}(t)$ distortion if compared to that resulting from the product of ϕ_{EXT0} value with selected R_{EXT} waveform ($R_{EXT}(t)$).

In summary, ϕ_{EXT} fluctuation alters significantly $P_{AW}(t)$ which is intended to be applied and makes it dependent on the respiratory characteristics of patient (R_P; C_P).

In order to maintain across the TVAPS the same level of steady flow (ϕ_{EXT0}) also during transient conditions, the STFGS puts into practice a compensation procedure as follows.

The ϕ_{EXT} is kept steady on controlled ϕ_{EXT0} value by modeling the ϕ_{VEN} waveform ($\phi_{VEN}(t)$) around ϕ_{VEN0} value on account of the instantaneous ϕ_{RES} and P_{EA} values as well as R_{EXT}/R_P ratio. The modeling of $\phi_{VEN}(t)$ intensity and shape during breathing is performed through the regulation around R_{G0} value of R_G.

As a result of theoretical treatment of the ALVS working principle, the analytical expression of R_G waveform ($R_G(t)$) required to successfully perform the compensation procedure during both inspiration and expiration has been determined within Section 4.1.

For an optimal matching between stationary and transient conditions the choice of ϕ_{VEN0} value and, as per relation (3), the choice of P_G and R_{G0} values should takes into account the maximum level expected for both ϕ_{INS} and ϕ_{EXP}.

The compensation procedure just described acts during the controlled breathing itself and it is based on feedback process minimizing the difference between current monitored and selected $P_{AW}(t)$. The compensation procedure, providing for steady and stabilized ϕ_{EXT} level during all the time of ventilation, makes possible the desired shape of $P_{AW}(t)$ excitation during both inspiration and expiration through an identical shape of $R_{EXT}(t)$.

The shape regulation of $R_{EXT}(t)$ above R_{EXT0} level, producing the desired $P_{AW}(t)$ is carried out considering the following relation:

$$P_{AW}(t) = \phi_{EXT0} R_{EXT}(t) \tag{8}$$

The intensity of $R_{EXT}(t)$ is controlled via feedback process minimizing the difference between required and measured tidal or minute volume delivered to the patient (dual control).

The feedback processes implemented for the compensation procedure and the tidal or minute volume control (DCV) are treated and described in Section 4.

The above-mentioned point (4) can be easily met with the implementation of particular $R_{EXT}(t)$. For instance, the patient can be treated with the conventional CPAP (continuous positive airways pressure) or BILEVEL/BIPAP (two levels of continuous positive airways pressure) ventilation setting R_{EXT} on a single constant value for all the time or on two different constant values for two consecutive time intervals, respectively. If required, the compensation procedure can be applied in these cases also.

The flow switches S1 and S2 are always kept "ON", allowing a continuous airflow crossing the TVAPS. This eliminates the transient effects on flow switching providing the optimal ventilation control as well as the spontaneous breathing compatibility.

The STFGS and the TVAPS can be disconnected at any time from the DRSS (patient) by switching "OFF" S1 and S2, respectively. By proper assessment of S1 and S2 closure time [25] the flow interruption technique is extremely useful for the instantaneous monitoring of static lung compliance and of both inspiratory and expiratory airways resistance as well as for the detection of intrinsic or auto positive end expiratory pressure [26].

This opportunity is particularly advantageous when nonlinear or unsteady respiratory mechanics is involved. Moreover, the flow interruption technique is the only procedure available for the monitoring of effective patient's respiratory parameters when more physiological waveforms as airways pressure excitation are employed [27]. Thus, in these both cases the results of theory developed in Section 4 cannot be applied to the purpose.

4. Theory of DCV optimization

The present chapter deals with the theory of DCV optimization developed for research and clinical applications. The theory is based on analytical treatment of the physical model implemented by the ALVS design.

The electrical-equivalent network of the ALVS (Fig. 3) used for analyzing and solving the theoretical problem is shown in the Fig. 4.

The rightness of the adoption of such model comes from the equivalent behaviour exhibited by fluidic and electrical circuits within the conditions and hypothesis defining the present work.

In this regard the basic hypothesis on respiratory mechanics from which the theoretical treatment will be here developed are described and discussed as follows.

The first hypothesis consists in considering the drop of pressure (ΔP) across any fluidic resistance (R) linearly dependent on flow (ϕ), according to the following relation:

$$\Delta P = R\phi \tag{9}$$

The validity of (9) implies that R is not dependent on ϕ, according to ideal laminar flow condition. With the exception of the airways resistance (R_P) belonging to the DRSS, all the ALVS resistances have been designed to operate in laminar flow condition. Considering that the flow condition across R_P is generally unpredictable, as well as ϕ_{RES} is a time varying quantity inside each single breathing, the real determination of effective R_P value is not an easy task. Nevertheless, the dependence of R_P on breathing time can be approximated with a bilevel (two constant levels) function representing the effective average value of R_P assumed during inspiratory

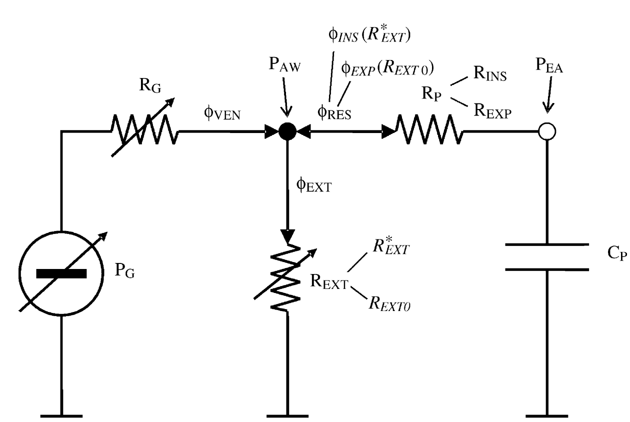

Fig. 4. Electrical-equivalent network of the ALVS.

and expiratory time, named inspiratory (R_{INS}) and expiratory (R_{EXP}) airways resistance, respectively [19,28]. Practically, R_{INS} and R_{EXP} correspond to the value of R_P obtained from (9) in which the average airflow values during inspiration (ϕ^0_{INS}) and expiration (ϕ^0_{EXP}) are considered, respectively. As it will be pointed out later (Section 4.3), ϕ^0_{INS} and ϕ^0_{EXP} equal the ratio of tidal volume (V_{TID}) to inspiratory (TI) and expiratory (TE) times, respectively.

The second hypothesis consists in considering over the whole duration of each single breathing the lung volume (V_P) linearly dependent on endoalveolar pressure (P_{EA}), according to the following relation:

$$V_P = C_P P_{EA} \tag{10}$$

C_P represents the proportional constant of the V_P–P_{EA} relationship called static lung compliance [29]. With reference to the time variation inside each single breathing the relation (10) implies that the ratio between V_P waveform ($V_P(t)$) and P_{EA} waveform ($P_{EA}(t)$) is not dependent on time but can be assumed constant, according to the following relation:

$$C_P = \frac{V_P(t)}{P_{EA}(t)} \tag{11}$$

The approximations just introduced on R_P (R_{INS}, R_{EXP}) and C_P, neglecting their time variation inside of each single breathing, are reasonable considering the particular physiopathologic and clinical condition occurring when DCV is applied to patient. Thus, the respiratory system of an healthy anaesthetized or severely brain injured patient in most cases exhibits a steady and reproducible response to controlled ventilation treatment over time intervals shorter than or equal to the breathing periods normally selected [29–31]. Moreover, according to the relation (10), the V_P–P_{EA} relationship can be assumed linear inside the breathing dynamics involved which is considerably reduced on account of small tidal volumes required [32,33].

Morphologic and physiopathologic modification of patient's respiratory system, drug therapy, changing of clinical staff options on ventilation parameters setting as $PEEP_{EXT}$ or tidal volume can induce R_P or/and C_P variations during the controlled ventilation treatment [27,34]. Nevertheless, such variations can be detected if we compare two different breathings as a whole, considering they do not involve the transient response inside of the single breathing but only the steady condition of the system reached at the end of both inspiration and expiration times.

The R_P or/and C_P variations between different breathings as a whole do not represent any problem to the ALVS functional performances since the ventilation control is optimized through the implementation of a specific closed-loop procedure adapting automatically the setting of inspiratory and expiratory times to the current value of both R_P or/and C_P and hence to the current value of respiratory time constant (Section 4.3). The detection and the measurement of any R_P or/and C_P variation occurring during the ventilation treatment is carried out by a diagnostic monitoring system dedicated to the purpose (Section 5).

Therefore, if a considerable change of inspiratory and expiratory times can be tolerated, the proposed method of ventilation control is theoretically available for most clinical conditions and patient's pathologies.

The effects of non-linearity on R_P or/and C_P behavior, occurring inside a single controlled breathing, cannot be ignored from a theoretical and experimental point of view if a certain amount of spontaneous breathing activity is present or in special clinical condition for which – instead of the square waveform – more refined waveforms as airways pressure excitation are applied in DCV, in order to attain specific therapeutic aims as alveolar recruitment [27,35–38].

The consequences of such effects on ALVS performances go beyond the subject of the present work and will be deeply investigated in the future when our research will be devoted to assisted/controlled ventilation with more physiological waveforms as airways pressure excitation along with spontaneous ventilation modalities.

Thus, considering all the above-mentioned considerations and in particular the relations (9)–(11), the electrical potential, current, charge, resistance and capacity of electrical circuits can be replaced by pressure, flow, volume, resistance and compliance of fluidic circuits, respectively. Moreover, theorems and methods usually employed for solving electrical network problems are available and in particular, Kirchhoff's laws give a powerful theoretical instrument to the purpose.

Observing the patient (DRSS) configuration it appears as an integration circuit leading to the well-known relationship between P_{AW} excitation and P_{EA} or ϕ_{RES} reaction.

4.1. Transient behavior of ALVS between two levels of airways pressure excitation

From Fig. 4, it is easy to understand how the inspiration and expiration can be both carried out by ALVS. Keeping constant P_G and R_G on their proper values required for $PEEP_{EXT}$ control (stationary conditions) the inspiration and the expiration can be triggered by switching R_{EXT} from a lower (R_{EXT0}) to an upper (R^*_{EXT}) value and vice versa, respectively.

For a square waveform as airways pressure excitation R_{EXT} must be kept on R^*_{EXT} and R_{EXT0} value until the end of inspiration and expiration, respectively.

The transient reaction of ALVS as a function of time during inspiration and expiration can be studied through the application of an appropriate method to the network of Fig. 4. The method based on transformation of Kirchhoff's equations from time (t) to Laplace (s) variable domains and vice versa (antitransformation) offers the best choice to our purpose.

Concerning the inspiration time, the application of both Kirchhoff's laws to the network of Fig. 4 leads to the following three equations:

$$\phi_{VENi}(s) = \phi_{EXTi}(s) + \phi_{INS}(s) \tag{12}$$

$$\frac{P_G}{s} = R_G\phi_{VENi}(s) + R^*_{EXT}\phi_{EXTi}(s) \tag{13}$$

$$\frac{P_G}{s} = R_G\phi_{VENi}(s) + \left(R_{INS} + \frac{1}{C_P s}\right)\phi_{INS}(s) + \frac{PEEP_{EXT}}{s} \tag{14}$$

The ratio $PEEP_{EXT}/s$ of the Eq. (14) takes into account the stationary conditions occurring at the beginning of inspiration time and thus at the end of last expiration time for which both the relations (3) and (4) can be applied. Considering that, the endoalveolar end expiratory pressure ($PEEP_{TOT}$) can be assumed equal to the stationary $PEEP_{EXT}$ value, according to the following expression:

$$P_{EAi}(0) = PEEP_{TOT} = P_{AWi}(0) = PEEP_{EXT} \tag{15}$$

The unknown functions $\phi_{INS}(s)$, $\phi_{VENi}(s)$ and $\phi_{EXTi}(s)$ can be determined combining properly the three Eqs. (12)–(14). The solution relative to $\phi_{INS}(s)$ assumes the following expression:

$$\phi_{INS}(s) = \frac{\beta_i}{\alpha_i}\frac{1}{s + a_i} \tag{16}$$

where

$$\beta_i = P_G R^*_{EXT} - PEEP_{EXT}(R_G + R^*_{EXT}) \tag{17}$$

$$\alpha_i = R_G R^*_{EXT} + R_G R_{INS} + R^*_{EXT} R_{INS} \tag{18}$$

$$a_i = \frac{R_G + R^*_{EXT}}{C_P\alpha_i} \tag{19}$$

Considering the relation (4) and occurring the condition $R^*_{EXT} > R_{EXT0}$ it is easy to demonstrate from (17) that β_i is always a positive quantity.

According to the Laplace's antitransformation of (16), the function $\phi_{INS}(t)$ assumes the following expression:

$$\phi_{INS}(t) = \frac{\beta_i}{\alpha_i}e^{-a_i t} \tag{20}$$

The inspiratory time constant (τ_{INS}), defined as the reciprocal of the pole a_i, from (19) it assumes the following expression:

$$\tau_{INS} = \frac{1}{a_i} = \frac{C_P\alpha_i}{R_G + R^*_{EXT}} \tag{21}$$

Going on with the same approach the following inspiratory flow and pressure waveforms can be obtained:

$$\phi_{VENi}(t) = \frac{P_G + R^*_{EXT}(\beta_i/\alpha_i)e^{-a_i t}}{R_G + R^*_{EXT}} \tag{22}$$

$$\phi_{EXTi}(t) = \frac{P_G - R_G(\beta_i/\alpha_i)e^{-a_i t}}{R_G + R^*_{EXT}} \tag{23}$$

$$P_{AWi}(t) = R^*_{EXT}\phi_{EXTi}(t) = \left(P_G - R_G\frac{\beta_i}{\alpha_i}e^{-a_i t}\right)\frac{R^*_{EXT}}{R_G + R^*_{EXT}} \tag{24}$$

$$P_{EAi}(t) = P_{AWi}(t) - R_{INS}\phi_{INS}(t) = \frac{P_G R^*_{EXT} - \beta_i e^{-a_i t}}{R_G + R^*_{EXT}} \tag{25}$$

Considering both the relations (11) and (25) the inspiratory waveform of lung volume ($V_{Pi}(t)$) results in the following expression:

$$V_{Pi}(t) = P_{EAi}(t)C_P = (P_G R^*_{EXT} - \beta_i e^{-a_i t})\frac{C_P}{R_G + R^*_{EXT}} \tag{26}$$

Assuming R_G constant in time and set on the equilibrium value (R_{G0}) required for $PEEP_{EXT}$ control together with considering the condition (4) and the relation (5), the expressions (17)–(26) can be adequately approximated with the followings, respectively:

$$\beta_i = P_G(R^*_{EXT} - R_{EXT0}) \tag{27}$$

$$\alpha_i = R_{G0}(R^*_{EXT} + R_{INS}) \tag{28}$$

$$a_i = \frac{1}{(R^*_{EXT} + R_{INS})C_P} \tag{29}$$

$$\phi_{INS}(t) = \phi_{VEN0}\frac{R^*_{EXT} - R_{EXT0}}{R^*_{EXT} + R_{INS}}e^{-(t/(R^*_{EXT}+R_{INS})C_P)} \tag{30}$$

$$\tau_{INS} = \frac{1}{a_i} = (R^*_{EXT} + R_{INS})C_P \tag{31}$$

$$\phi_{VENi}(t) = \phi_{VEN0} \tag{32}$$

$$\phi_{EXTi}(t) = \phi_{VEN0} - \phi_{INS}(t) \tag{33}$$

$$P_{AWi}(t) = P_{GI} - R^*_{EXT}\phi_{INS}(t) \tag{34}$$

$$P_{EAi}(t) = P_{GI} - (R^*_{EXT} + R_{INS})\phi_{INS}(t) \tag{35}$$

$$V_{Pi}(t) = [P_{GI} - (R^*_{EXT} + R_{INS})\phi_{INS}(t)]C_P \tag{36}$$

The inspiratory waveforms of ventilation parameters (30), (32)–(36) along with of ALVS components output (P_G; R_G; R_{EXT}) are reported in the Fig. 5 with continuous lines.

Concerning the expiration time, the application of both Kirchhoff's laws to the network of Fig. 4 leads to the following three equations:

$$\phi_{VENe}(s) = \phi_{EXTe}(s) - \phi_{EXP}(s) \tag{37}$$

$$\frac{P_G}{s} = R_G\phi_{VENe}(s) + R_{EXT0}\phi_{EXTe}(s) \tag{38}$$

$$\frac{P_G}{s} = R_G\phi_{VENe}(s) - \left(R_{EXP} + \frac{1}{C_P s}\right)\phi_{EXP}(s) + \frac{P_{GI}}{s} \tag{39}$$

The ratio P_{GI}/s of the Eq. (39) takes into account the stationary conditions occurring at the beginning of expiration time and thus at the end of last inspiration time for which both the relations (3) and (7) can be applied. Considering that, the endoalveolar end inspiratory pressure ($P_{EAe}(0)$) can

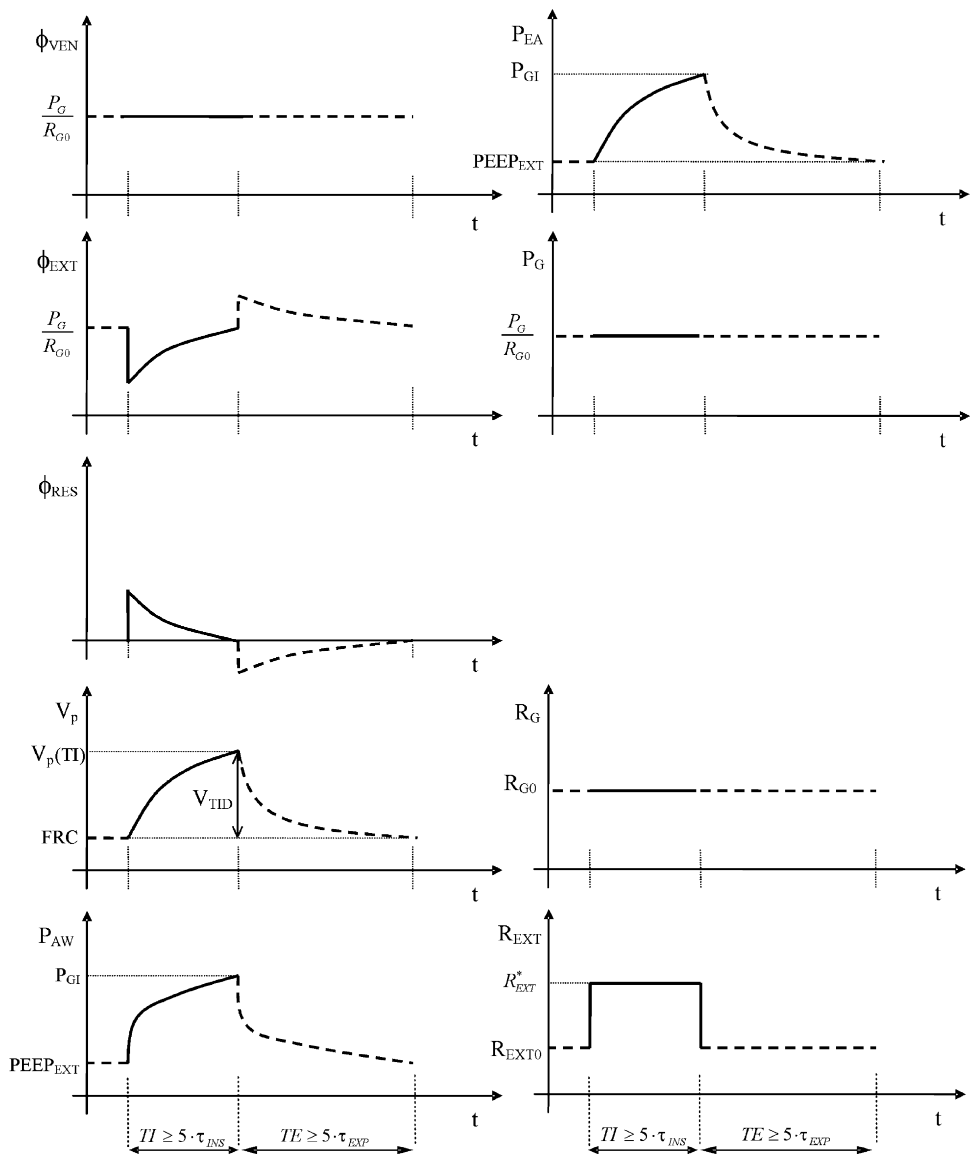

Fig. 5. Time-waveform of ventilation parameters (ϕ_{VEN}; ϕ_{EXT}; ϕ_{RES}; V_{P}; P_{AW}; P_{EA}) and of ALVS components output (P_{G}; R_{G}; R_{EXT}) in uncompensated dual-controlled ventilation with square waveform as airways pressure (P_{AW}) excitation. The inspiration and expiration waveforms are reported with continuous and dashed lines, respectively. See text.

be assumed equal to the stationary P_{GI} value, according to the following expression:

$$P_{\text{EAe}}(0) = P_{\text{AWe}}(0) = P_{\text{GI}} \tag{40}$$

The unknown functions $\phi_{\text{EXP}}(s)$, $\phi_{\text{VENe}}(s)$ and $\phi_{\text{EXTe}}(s)$ can be determined combining properly the three Eqs. (38)–(40). The solution relative to $\phi_{\text{EXP}}(s)$ assumes the following expression:

$$\phi_{\text{EXP}}(s) = \frac{\beta_{\text{e}}}{\alpha_{\text{e}}}\frac{1}{s + a_{\text{e}}} \tag{41}$$

where

$$\beta_{\text{e}} = P_{\text{GI}}(R_{\text{G}} + R_{\text{EXT0}}) - P_{\text{G}}R_{\text{EXT0}} \tag{42}$$

$$\alpha_{\text{e}} = R_{\text{G}}R_{\text{EXT0}} + R_{\text{G}}R_{\text{EXP}} + R_{\text{EXT0}}R_{\text{EXP}} \tag{43}$$

$$a_{\text{e}} = \frac{R_{\text{G}} + R_{\text{EXT0}}}{C_{\text{P}}\alpha_{\text{e}}} \tag{44}$$

Considering the relation (7) and occurring the condition $R^*_{\text{EXT}} > R_{\text{EXT0}}$ it is easy to demonstrate from (42) that β_{e} is always a positive quantity.

According to the Laplace's antitransformation of (41), the function $\phi_{\text{EXP}}(t)$ assumes the following expression:

$$\phi_{\text{EXP}}(t) = \frac{\beta_{\text{e}}}{\alpha_{\text{e}}}\mathrm{e}^{-a_{\text{e}}t} \tag{45}$$

The expiratory time constant (τ_{EXP}), defined as the reciprocal of the pole a_{e}, from (44) it assumes the following expression:

$$\tau_{\text{EXP}} = \frac{1}{a_{\text{e}}} = \frac{C_{\text{P}}\alpha_{\text{e}}}{R_{\text{G}} + R_{\text{EXT0}}} \tag{46}$$

Going on with the same approach the following expiratory flow and pressure waveforms can be obtained:

$$\phi_{\mathrm{VENe}}(t)=\frac{P_{\mathrm{G}}-R_{\mathrm{EXT0}}(\beta_{\mathrm{e}}/\alpha_{\mathrm{e}})\mathrm{e}^{-a_{\mathrm{e}}t}}{R_{\mathrm{G}}+R_{\mathrm{EXT0}}} \tag{47}$$

$$\phi_{\mathrm{EXTe}}(t)=\frac{P_{\mathrm{G}}+R_{\mathrm{G}}(\beta_{\mathrm{e}}/\alpha_{\mathrm{e}})\mathrm{e}^{-a_{\mathrm{e}}t}}{R_{\mathrm{G}}+R_{\mathrm{EXT0}}} \tag{48}$$

$$\begin{aligned}P_{\mathrm{AWe}}(t)&=R_{\mathrm{EXT0}}\phi_{\mathrm{EXTe}}(t)\\&=\left(P_{\mathrm{G}}+R_{\mathrm{G}}\frac{\beta_{\mathrm{e}}}{\alpha_{\mathrm{e}}}\mathrm{e}^{-a_{\mathrm{e}}t}\right)\frac{R_{\mathrm{EXT0}}}{R_{\mathrm{G}}+R_{\mathrm{EXT0}}}\end{aligned} \tag{49}$$

$$\begin{aligned}P_{\mathrm{EAe}}(t)&=P_{\mathrm{AWe}}(t)+R_{\mathrm{EXP}}\phi_{\mathrm{EXP}}(t)\\&=\frac{P_{\mathrm{G}}R_{\mathrm{EXT0}}+\beta_{\mathrm{e}}\,\mathrm{e}^{-a_{\mathrm{e}}t}}{R_{\mathrm{G}}+R_{\mathrm{EXT0}}}\end{aligned} \tag{50}$$

Considering both the relations (11) and (50) the expiratory waveform of lung volume ($V_{\mathrm{Pe}}(t)$) results in the following expression:

$$\begin{aligned}V_{\mathrm{Pe}}(t)&=P_{\mathrm{EAe}}(t)C_{\mathrm{P}}\\&=(P_{\mathrm{G}}R_{\mathrm{EXT0}}+\beta_{\mathrm{e}}\,\mathrm{e}^{-a_{\mathrm{e}}t})\frac{C_{\mathrm{P}}}{R_{\mathrm{G}}+R_{\mathrm{EXT0}}}\end{aligned} \tag{51}$$

Assuming R_{G} constant in time and set on the equilibrium value (R_{G0}) required for $\mathrm{PEEP_{EXT}}$ control together with considering the condition (4) and the relation (7), the expressions (42)–(51) can be adequately approximated with the followings, respectively:

$$\beta_{\mathrm{e}}=P_{\mathrm{G}}(R^{*}_{\mathrm{EXT}}-R_{\mathrm{EXT0}}) \tag{52}$$

$$\alpha_{\mathrm{e}}=R_{\mathrm{G0}}(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}}) \tag{53}$$

$$a_{\mathrm{e}}=\frac{1}{(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}})C_{\mathrm{P}}} \tag{54}$$

$$\phi_{\mathrm{EXP}}(t)=\phi_{\mathrm{VEN0}}\frac{R^{*}_{\mathrm{EXT}}-R_{\mathrm{EXT0}}}{R_{\mathrm{EXT0}}+R_{\mathrm{EXP}}}\mathrm{e}^{-(t/(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}})C_{\mathrm{P}})} \tag{55}$$

$$\tau_{\mathrm{EXP}}=\frac{1}{a_{\mathrm{e}}}=(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}})C_{\mathrm{P}} \tag{56}$$

$$\phi_{\mathrm{VENe}}(t)=\phi_{\mathrm{VEN0}} \tag{57}$$

$$\phi_{\mathrm{EXTe}}(t)=\phi_{\mathrm{VEN0}}+\phi_{\mathrm{EXP}}(t) \tag{58}$$

$$P_{\mathrm{AWe}}(t)=\mathrm{PEEP_{EXT}}+R_{\mathrm{EXT0}}\phi_{\mathrm{EXP}}(t) \tag{59}$$

$$P_{\mathrm{EAe}}(t)=\mathrm{PEEP_{EXT}}+(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}})\phi_{\mathrm{EXP}}(t) \tag{60}$$

$$V_{\mathrm{Pe}}(t)=[\mathrm{PEEP_{EXT}}+(R_{\mathrm{EXT0}}+R_{\mathrm{EXP}})\phi_{\mathrm{EXP}}(t)]C_{\mathrm{P}} \tag{61}$$

The expiratory waveforms of ventilation parameters (55), (57)–(61) along with of ALVS components output (P_{G}; R_{G}; R_{EXT}) are reported in the Fig. 5 with dashed lines.

Finally, the respiratory time constant (τ_{RES}), defined as the sum of τ_{INS} and τ_{EXP}, can be obtained considering both the relations (31) and (56):

$$\tau_{\mathrm{RES}}=\tau_{\mathrm{INS}}+\tau_{\mathrm{EXP}}=(R^{*}_{\mathrm{EXT}}+R_{\mathrm{EXT0}}+R_{\mathrm{INS}}+R_{\mathrm{EXP}})C_{\mathrm{P}} \tag{62}$$

4.2. Compensation procedure

The rationale of the compensation procedure is the elimination of $P_{\mathrm{AW}}(t)$ distortion occurring during patient's breathing activity.

As introduced in Section 3, the compensation procedure consists in keeping for all the time of ventilation the flow crossing the TVAPS (ϕ_{EXT}) on a steady and stabilized level ($\phi_{\mathrm{EXT}}=\phi_{\mathrm{VEN0}}$).

The analytical expression of $P_{\mathrm{AW}}(t)$ distortion occurred when ALVS is set for inducing a square waveform as P_{AW} excitation has been carried out in Section 4.1. In particular, the expressions (34) and (59) relate to inspiratory ($P_{\mathrm{AWi}}(t)$) and expiratory ($P_{\mathrm{AWe}}(t)$) non compensated $P_{\mathrm{AW}}(t)$, respectively.

The elimination of $P_{\mathrm{AW}}(t)$ distortion is essential not only for carrying out the real $P_{\mathrm{AW}}(t)$ intended to be applied but particularly since it allows the useful implementation of the results available from simplified theory. This is very advantageous for the correct determination of critical parameters as respiratory characteristics of patient (diagnostic parameters), respiratory time constant as so on, all together providing for the optimization setting of ventilation treatments.

The analytical treatment and the working principles of the compensation procedure performed by the ALVS will be presented here in the case of advanced DCV with square waveform as P_{AW} excitation.

The compensated variables will be denoted with a specific apex character ($\wedge$).

Referring to the Fig. 4, the condition to be satisfied during the inspiratory time is the following:

$$\phi^{\wedge}_{\mathrm{EXTi}}=\frac{P_{\mathrm{G}}}{R_{\mathrm{G0}}}=\phi_{\mathrm{VEN0}} \tag{63}$$

From the condition (63), the following expression results:

$$P^{\wedge}_{\mathrm{AWi}}=R^{*}_{\mathrm{EXT}}\phi^{\wedge}_{\mathrm{EXTi}}=R^{*}_{\mathrm{EXT}}\frac{P_{\mathrm{G}}}{R_{\mathrm{G0}}}=R^{*}_{\mathrm{EXT}}\phi_{\mathrm{VEN0}} \tag{64}$$

The second Kirchhoff's law applied in the Laplace domain (s) to the DRSS (patient) circuit assumes the following expression:

$$\frac{P^{\wedge}_{\mathrm{AWi}}}{s}-\frac{1+C_{\mathrm{P}}s}{C_{\mathrm{P}}s}\phi^{\wedge}_{\mathrm{INS}}(s)-\frac{\mathrm{PEEP_{EXT}}}{s}=0 \tag{65}$$

The solution of the Eq. (65) consists in the following expression:

$$\phi^{\wedge}_{\mathrm{INS}}(s)=\phi_{\mathrm{VEN0}}\frac{R^{*}_{\mathrm{EXT}}-R_{\mathrm{EXT0}}}{R_{\mathrm{INS}}}\frac{1}{s+(1/R_{\mathrm{INS}}C_{\mathrm{P}})} \tag{66}$$

The expression (66) in the time (t) domain assumes the following expression:

$$\phi^{\wedge}_{\mathrm{INS}}(t)=\phi_{\mathrm{VEN0}}\frac{R^{*}_{\mathrm{EXT}}-R_{\mathrm{EXT0}}}{R_{\mathrm{INS}}}\mathrm{e}^{-(t/R_{\mathrm{INS}}C_{\mathrm{P}})} \tag{67}$$

From (67), the compensated inspiratory time constant ($\tau^{\wedge}_{\mathrm{INS}}$) results as follows:

$$\tau^{\wedge}_{\mathrm{INS}} = R_{\mathrm{INS}} C_{\mathrm{P}} \tag{68}$$

The first Kirchhoff's law applied to the airways node produces the following equation:

$$\phi^{\wedge}_{\mathrm{VENi}}(t) = \phi^{\wedge}_{\mathrm{EXTi}} + \phi^{\wedge}_{\mathrm{INS}}(t) = \phi_{\mathrm{VEN0}} + \phi^{\wedge}_{\mathrm{INS}}(t) \tag{69}$$

Combining (67) with (69) the following expression results:

$$\phi^{\wedge}_{\mathrm{VENi}}(t) = \phi_{\mathrm{VEN0}} \left(1 + \frac{R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}}}{R_{\mathrm{INS}}}\right) \mathrm{e}^{-(t/R_{\mathrm{INS}} C_{\mathrm{P}})} \tag{70}$$

The second Kirchhoff's law applied to the left loop (generator circuit) of the network of Fig. 4 produces the following equation:

$$P_{\mathrm{G}} - R^{\wedge}_{\mathrm{Gi}}(t)\phi^{\wedge}_{\mathrm{VENi}}(t) - P^{\wedge}_{\mathrm{AWi}} = 0 \tag{71}$$

where $R^{\wedge}_{\mathrm{Gi}}(t)$ is the R_{G} waveform to be implemented for performing the compensation procedure during inspiratory time. From (64), (70) and (71) it assumes the following expression:

$$R^{\wedge}_{\mathrm{Gi}}(t) = \frac{R_{\mathrm{INS}} R_{\mathrm{G0}}}{R_{\mathrm{INS}} + (R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}})} \mathrm{e}^{-(t/R_{\mathrm{INS}} C_{\mathrm{P}})} \tag{72}$$

Referring again to the Fig. 4, the condition to be satisfied during the expiratory time is the following:

$$\phi^{\wedge}_{\mathrm{EXTe}} = \frac{P_{\mathrm{G}}}{R_{\mathrm{G0}}} = \phi_{\mathrm{VEN0}} \tag{73}$$

From the condition (73), the following expression results:

$$P^{\wedge}_{\mathrm{AWe}} = R_{\mathrm{EXT0}} \phi^{\wedge}_{\mathrm{EXTe}} = R_{\mathrm{EXT0}} \frac{P_{\mathrm{G}}}{R_{\mathrm{G0}}} = R_{\mathrm{EXT0}} \phi_{\mathrm{VEN0}} \tag{74}$$

The second Kirchhoff's law applied in the Laplace domain (s) to the DRSS (patient) circuit assumes the following expression:

$$\frac{P^{\wedge}_{\mathrm{AWe}}}{s} + \left(\frac{1 + C_{\mathrm{P}} s}{C_{\mathrm{P}} s}\right) \phi^{\wedge}_{\mathrm{EXP}}(s) - \frac{P_{\mathrm{GI}}}{s} \tag{75}$$

The solution of the Eq. (75) consists in the following expression:

$$\phi^{\wedge}_{\mathrm{EXP}}(s) = \phi_{\mathrm{VEN0}} \frac{R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}}}{R_{\mathrm{EXP}}} \frac{1}{s + (1/R_{\mathrm{EXP}} C_{\mathrm{P}})} \tag{76}$$

The expression (76) in the time (t) domain assumes the following expression:

$$\phi^{\wedge}_{\mathrm{EXP}}(t) = \phi_{\mathrm{VEN0}} \frac{R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}}}{R_{\mathrm{EXP}}} \mathrm{e}^{-(t/R_{\mathrm{EXP}} C_{\mathrm{P}})} \tag{77}$$

From (77), the compensated expiratory time constant ($\tau^{\wedge}_{\mathrm{EXP}}$) results as follows:

$$\tau^{\wedge}_{\mathrm{EXP}} = R_{\mathrm{EXP}} C_{\mathrm{P}} \tag{78}$$

The first Kirchhoff's law applied to the airways node produces the following equation:

$$\phi^{\wedge}_{\mathrm{VENe}}(t) = \phi^{\wedge}_{\mathrm{EXTe}} - \phi^{\wedge}_{\mathrm{EXP}}(t) = \phi_{\mathrm{VEN0}} - \phi^{\wedge}_{\mathrm{EXP}}(t) \tag{79}$$

Combining (77) with (79) the following expression results:

$$\phi^{\wedge}_{\mathrm{VENe}}(t) = \phi_{\mathrm{VEN0}} \left(1 - \frac{R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}}}{R_{\mathrm{EXP}}}\right) \mathrm{e}^{-(t/R_{\mathrm{EXP}} C_{\mathrm{P}})} \tag{80}$$

The second Kirchhoff's law applied to the left loop (generator circuit) of the network of Fig. 4 produces the following equation:

$$P_{\mathrm{G}} - R^{\wedge}_{\mathrm{Ge}}(t)\phi^{\wedge}_{\mathrm{VENe}}(t) - P^{\wedge}_{\mathrm{AWe}} = 0 \tag{81}$$

where $R^{\wedge}_{\mathrm{Ge}}(t)$ is the R_{G} waveform to be implemented for performing the compensation procedure during expiratory time. From (74), (80) and (81) it assumes the following expression:

$$R^{\wedge}_{\mathrm{Ge}}(t) = \frac{R_{\mathrm{EXP}} R_{\mathrm{G0}}}{R_{\mathrm{EXP}} - (R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}})} \mathrm{e}^{-(t/R_{\mathrm{EXP}} C_{\mathrm{P}})} \tag{82}$$

Finally, the compensated respiratory time constant ($\tau^{\wedge}_{\mathrm{RES}}$) can be obtained considering both the relations (68) and (78), as follows:

$$\tau^{\wedge}_{\mathrm{RES}} = \tau^{\wedge}_{\mathrm{INS}} + \tau^{\wedge}_{\mathrm{EXP}} = (R_{\mathrm{INS}} + R_{\mathrm{EXP}}) C_{\mathrm{P}} \tag{83}$$

In conclusion, through the implementation of (72) and (82) during the inspiration and expiration time, respectively, the STFGS keeps ϕ_{EXT} on a steady value over time insensitive to both shape and intensity of ϕ_{RES} waveform ($\phi_{\mathrm{RES}}(t)$). In such a way, a perfect square waveform as P_{AW} excitation stable and insensitive to the load (DRSS/patient) characteristics (R_{P}; C_{P}) can be carried out by the TVAPS.

The effects on waveform shape and intensity of ventilation parameters induced by the application of the compensation procedure when a square waveform as airways pressure excitation is selected will be described in the next chapter (Section 4.3).

With the same working principles just described, the compensation procedure can be successfully applied to let any $P_{\mathrm{AW}}(t)$ of experimental or clinical interest become stable and insensitive to the load.

In order to approach a more physiological $P_{\mathrm{AW}}(t)$ shape if P_{AW} is linearly increased during inspiratory time, it is possible to demonstrate that, after about three inspiratory time constants, P_{EA} increase is linear in time with the same slope selected for P_{AW}.

When the $P_{\mathrm{AW}}(t)$ shape is changed during the breathing time the ventilation control is dependent on the final state reached by the system before the change as well as on current $P_{\mathrm{AW}}(t)$.

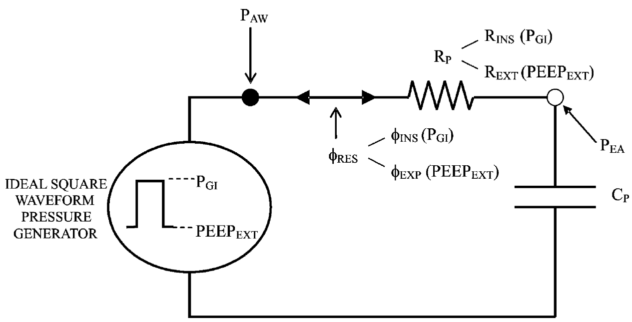

Fig. 6. Equivalent circuit of an ideal square waveform pressure generator connected to the patient's airways.

4.3. Compensated square waveform as airways pressure excitation

As described in Section 3, the conventional PCV consists in the application to patient's airways of two different constant and stabilized pressure levels during inspiration (P_{GI}) and expiration ($\mathrm{PEEP}_{\mathrm{EXT}}$). Such perfect square waveform as P_{AW} excitation could be carried out by connecting the patient with an ideal square waveform P_{AW} generator like that realized by the combination of STFGS with TVAPS (Section 4.2). The equivalent circuit of such P_{AW} generator connected to the load (DRSS/patient) is shown in the Fig. 6.

In controlled breathing condition both R_{INS} and R_{EXP} as well as C_{P} can be assumed as constant parameters. Thus, in summary, referring to the Fig. 6, given the same C_{P} value, during inspiration and expiration P_{AW} is on the upper (P_{GI}) and lower level ($\mathrm{PEEP}_{\mathrm{EXT}}$), R_{P} assumes its inspiratory (R_{INS}) and expiratory (R_{EXP}) value, while ϕ_{INS} and ϕ_{EXP} denote the inspiratory and expiratory ϕ_{RES} components, respectively.

In Section 4.2, the analytical expression of flow waveforms and time constant during inspiration ($\phi^{\wedge}_{\mathrm{INS}}(t)$, $\phi^{\wedge}_{\mathrm{EXTi}}(t)$, $\phi^{\wedge}_{\mathrm{VENi}}(t)$, $\tau^{\wedge}_{\mathrm{INS}}$) and expiration ($\phi^{\wedge}_{\mathrm{EXP}}(t)$, $\phi^{\wedge}_{\mathrm{EXTe}}(t)$, $\phi^{\wedge}_{\mathrm{VENe}}(t)$, $\tau^{\wedge}_{\mathrm{EXP}}$) have been obtained as a result of the theoretical treatment of compensated square waveform P_{AW} excitation.

4.3.1. Inspiration time

Taking into account both the relations (4) and (7), the expression (67) can be arranged as follows:

$$\phi^{\wedge}_{\mathrm{INS}}(t) = \left(\frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{INS}}}\right) \mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{INS}})} \tag{84}$$

The application of the second Kirchhoff's law to the circuit of Fig. 6 provides the following equations:

$$P^{\wedge}_{\mathrm{EAi}}(t) = P^{\wedge}_{\mathrm{AWi}}(t) - R_{\mathrm{INS}}\phi^{\wedge}_{\mathrm{INS}}(t) \tag{85}$$

By inserting both the (64) and (84) into the (85), the following equation results:

$$\begin{aligned} P^{\wedge}_{\mathrm{EAi}}(t) &= \phi_{\mathrm{VEN0}}[R^{*}_{\mathrm{EXT}} - (R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}})\mathrm{e}^{-(t/R_{\mathrm{INS}}C_{\mathrm{P}})}] \\ &= P_{\mathrm{GI}} - (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{INS}})} \end{aligned} \tag{86}$$

The analytical expression of compensated waveform of inspiratory lung volume ($V^{\wedge}_{\mathrm{Pi}}(t)$) can be determined considering both the Eq. (86) and the relation (11), as follows:

$$\begin{aligned} V^{\wedge}_{\mathrm{Pi}}(t) &= C_{\mathrm{P}}\phi_{\mathrm{VEN0}}[R^{*}_{\mathrm{EXT}} - (R^{*}_{\mathrm{EXT}} - R_{\mathrm{EXT0}})\mathrm{e}^{-(t/R_{\mathrm{INS}}C_{\mathrm{P}})}] \\ &= C_{\mathrm{P}}[P_{\mathrm{GI}} - (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{INS}})}] \end{aligned} \tag{87}$$

According to (11), the initial value of $V^{\wedge}_{\mathrm{Pi}}(t)$ ($V^{\wedge}_{\mathrm{Pi}}(0)$), corresponding to the functional residual capacity (FRC), can be obtained by setting $t = 0$ in (87):

$$V^{\wedge}_{\mathrm{Pi}}(0) = \mathrm{FRC} = C_{\mathrm{P}}\mathrm{PEEP}_{\mathrm{EXT}} \tag{88}$$

If the upper (P_{GI}) level of P_{AW} square waveform is kept for an inspiration time (TI) of about five times $\tau^{\wedge}_{\mathrm{INS}}$ ($\mathrm{TI} = 5\tau^{\wedge}_{\mathrm{INS}}$), then as it is well known, (84), (86) and (87) become, respectively:

$$\phi^{\wedge}_{\mathrm{INS}}(5\tau^{\wedge}_{\mathrm{INS}}) = \left(\frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{INS}}}\right) \mathrm{e}^{-5} \approx 0 \tag{89}$$

$$P^{\wedge}_{\mathrm{EAi}}(5\tau^{\wedge}_{\mathrm{INS}}) = P_{\mathrm{GI}} - (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-5} \approx P_{\mathrm{GI}} \tag{90}$$

$$V^{\wedge}_{\mathrm{Pi}}(5\tau^{\wedge}_{\mathrm{INS}}) = C_{\mathrm{P}}[P_{\mathrm{GI}} - (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-5}] \approx C_{\mathrm{P}} P_{\mathrm{GI}} \tag{91}$$

Therefore, the measurement of the time required for reaching the end of transient inspiration time (TI^{*}), i.e. for observing a ninety nine per cent (99%) reduction of $\phi^{\wedge}_{\mathrm{INS}}$ with regard to its initial value ($\phi^{\wedge}_{\mathrm{INS}}(0)$) is useful for the determination of $\tau^{\wedge}_{\mathrm{INS}}$, as stated by the following expression:

$$\tau^{\wedge}_{\mathrm{INS}} = \frac{\mathrm{TI}^{*}}{5} \tag{92}$$

$\phi^{\wedge}_{\mathrm{INS}}(0)$ can be detected as the initial (peak) value of $\phi^{\wedge}_{\mathrm{INS}}(t)$, according to the result obtained by setting $t = 0$ in (84):

$$\phi^{\wedge}_{\mathrm{INS}}(0) = \frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{INS}}} \tag{93}$$

According to (90), a time of inspiration (TI) equal (or greater) to TI^{*} is powerful also for the determination of the real peak value of $P^{\wedge}_{\mathrm{EA}}$ reached at the end of inspiration, as it equals P_{GI}.

According to (69), $\phi^{\wedge}_{\mathrm{INS}}(t)$ can be detected by the ALVS monitoring system as the difference between $\phi^{\wedge}_{\mathrm{VENi}}(t)$ and $\phi^{\wedge}_{\mathrm{EXTi}}(t)$.

Considering that $\phi^{\wedge}_{\mathrm{INS}}(t)$ is defined as the time derivation of $V^{\wedge}_{\mathrm{Pi}}(t)$:

$$\phi^{\wedge}_{\mathrm{INS}}(t) = \frac{\mathrm{d}V^{\wedge}_{\mathrm{Pi}}(t)}{\mathrm{d}t} \tag{94}$$

$V^{\wedge}_{\mathrm{Pi}}(\mathrm{TI})$ can be determined through the time integration of (84) from 0 to TI, according to the following expression:

$$V^{\wedge}_{\mathrm{Pi}}(\mathrm{TI}) = V^{\wedge}_{\mathrm{Pi}}(0) + \int_0^{\mathrm{TI}} \phi^{\wedge}_{\mathrm{INS}}(t)\,\mathrm{d}t = \mathrm{FRC} + V^{\wedge}_{\mathrm{TIDi}} \tag{95}$$

The equivalence between the second and the third members of (95) takes into account the relation (88) as well as the definition of inspiratory tidal volume ($V^{\wedge}_{\mathrm{TIDi}}$), as follows:

$$V^{\wedge}_{\mathrm{TIDi}} = \int_0^{\mathrm{TI}} \phi^{\wedge}_{\mathrm{INS}}(t)\,\mathrm{d}t \tag{96}$$

The detection of $V^{\wedge}_{\mathrm{TIDi}}$ is performed by the ALVS monitoring system through the implementation of (96).

Considering the set of expression (11), (88), (90), (95) and (96) with a time of inspiration equal to TI*, the following relation results:

$$C^{\wedge}_{\mathrm{P}} = \frac{V^{\wedge *}_{\mathrm{TIDi}}}{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}} \tag{97}$$

where $V^{\wedge *}_{\mathrm{TIDi}}$, according to (96), is the tidal volume collected during an inspiration lasting a time equal to TI*.

Once C_{P} has been determined by means of (97), FRC and R_{INS} can be obtained from (88) and (68) along with (92), respectively.

The expression (93) provides an alternative way for the determination of R_{INS}.

4.3.2. Expiration time

Taking into account both the relations (4) and (7), the expression (77) can be arranged as follows:

$$\phi^{\wedge}_{\mathrm{EXP}}(t) = \left(\frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{EXP}}}\right) \mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{EXP}})} \tag{98}$$

The application of the second Kirchhoff's law to the circuit of Fig. 6 provides the following equations:

$$P^{\wedge}_{\mathrm{EAe}}(t) = P^{\wedge}_{\mathrm{AWe}}(t) + R_{\mathrm{EXP}}\phi^{\wedge}_{\mathrm{EXP}}(t) \tag{99}$$

By inserting both the (74) and (98) into the (99), the following equation results:

$$\begin{aligned} P^{\wedge}_{\mathrm{EAe}}(t) &= \phi_{\mathrm{VEN0}}[R_{\mathrm{EXT0}} + (R^*_{\mathrm{EXT}} - R_{\mathrm{EXT0}})\mathrm{e}^{-(t/R_{\mathrm{EXP}}C_{\mathrm{P}})}] \\ &= P_{\mathrm{EAe}}(t) = \mathrm{PEEP}_{\mathrm{EXT}} + (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{EXP}})} \end{aligned} \tag{100}$$

The analytical expression of compensated waveform of expiratory lung volume ($V^{\wedge}_{\mathrm{Pe}}(t)$) can be determined considering both the Eq. (100) and the relation (11), as follows:

$$\begin{aligned} V^{\wedge}_{\mathrm{Pe}}(t) &= C_{\mathrm{P}}\phi_{\mathrm{VEN0}}[R_{\mathrm{EXT0}} + (R^*_{\mathrm{EXT}} - R_{\mathrm{EXT0}})\mathrm{e}^{-(t/R_{\mathrm{EXP}}C_{\mathrm{P}})}] \\ &= C_{\mathrm{P}}P^{\wedge}_{\mathrm{EAe}}(t) \\ &= C_{\mathrm{P}}[\mathrm{PEEP}_{\mathrm{EXT}} + (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-(t/\tau^{\wedge}_{\mathrm{EXP}})}] \end{aligned} \tag{101}$$

According to (11), the initial value of $V^{\wedge}_{\mathrm{Pe}}(t)$ ($V^{\wedge}_{\mathrm{Pe}}(0)$) can be obtained by setting $t = 0$ in (101):

$$V^{\wedge}_{\mathrm{Pe}}(0) = V^{\wedge}_{\mathrm{Pi}}(\mathrm{TI}^*) = C_{\mathrm{P}}P_{\mathrm{GI}} \tag{102}$$

If the lower ($\mathrm{PEEP}_{\mathrm{EXT}}$) level of P_{AW} square waveform is kept for an expiration time (TE) of about five times $\tau^{\wedge}_{\mathrm{EXP}}$ ($\mathrm{TE} = 5\tau^{\wedge}_{\mathrm{EXP}}$), then as it is well known (98), (100) and (101) become, respectively:

$$\phi^{\wedge}_{\mathrm{EXP}}(5\tau^{\wedge}_{\mathrm{EXP}}) = \left(\frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{EXP}}}\right)\mathrm{e}^{-5} \approx 0 \tag{103}$$

$$\begin{aligned} P^{\wedge}_{\mathrm{EAe}}(5\tau^{\wedge}_{\mathrm{EXP}}) &= [\mathrm{PEEP}_{\mathrm{EXT}} + (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-5}] \\ &\approx \mathrm{PEEP}_{\mathrm{EXT}} \end{aligned} \tag{104}$$

$$\begin{aligned} V^{\wedge}_{\mathrm{Pe}}(5\tau^{\wedge}_{\mathrm{EXP}}) &= C_{\mathrm{P}}[\mathrm{PEEP}_{\mathrm{EXT}} + (P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}})\mathrm{e}^{-5}] \\ &\approx C_{\mathrm{P}}\mathrm{PEEP}_{\mathrm{EXT}} = \mathrm{FRC} \end{aligned} \tag{105}$$

Therefore, the measurement of the time required for reaching the end of transient expiration time (TE*), i.e. for observing a ninety-nine per cent (99%) reduction of $\phi^{\wedge}_{\mathrm{EXP}}$ with regard to its initial value ($\phi^{\wedge}_{\mathrm{EXP}}(0)$) is useful for the determination of $\tau^{\wedge}_{\mathrm{EXP}}$, as stated by the following expression:

$$\tau^{\wedge}_{\mathrm{EXP}} = \frac{\mathrm{TE}^*}{5} \tag{106}$$

$\phi^{\wedge}_{\mathrm{EXP}}(0)$ can be detected as the initial (peak) value of $\phi^{\wedge}_{\mathrm{EXP}}(t)$, according to the result obtained by setting $t = 0$ in (98):

$$\phi^{\wedge}_{\mathrm{INS}}(0) = \frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{R_{\mathrm{INS}}} \tag{107}$$

Combining (93) with (107) the following expression results:

$$\frac{R_{\mathrm{EXP}}}{R_{\mathrm{INS}}} = \frac{\phi^{\wedge}_{\mathrm{INS}}(0)}{\phi^{\wedge}_{\mathrm{EXP}}(0)} \tag{108}$$

So, from (108), the ratio between two monitored quantities provides the evaluation of $R_{\mathrm{EXP}}/R_{\mathrm{INS}}$ ratio useful for diagnostic purpose.

According to (104), a time of expiration (TE) equal (or greater) to TE* is powerful also for avoiding intrinsic or auto positive end expiratory pressure ($\mathrm{PEEP}_{\mathrm{AUTO}}$) consisting in a value of P_{EA} at the end of expiration ($\mathrm{PEEP}_{\mathrm{TOT}}$) greater than $\mathrm{PEEP}_{\mathrm{EXT}}$ ($\mathrm{PEEP}_{\mathrm{AUTO}} = \mathrm{PEEP}_{\mathrm{TOT}} - \mathrm{PEEP}_{\mathrm{EXT}}$).

According to (79), $\phi^{\wedge}_{\mathrm{EXP}}(t)$ can be detected by the ALVS monitoring system as the difference between $\phi^{\wedge}_{\mathrm{EXTe}}(t)$ and $\phi^{\wedge}_{\mathrm{VENe}}(t)$.

Considering that $\phi^{\wedge}_{\mathrm{EXP}}(t)$ is defined as the negative time derivation of $V^{\wedge}_{\mathrm{Pe}}(t)$:

$$\phi^{\wedge}_{\mathrm{EXP}}(t) = -\frac{\mathrm{d}V^{\wedge}_{\mathrm{Pe}}(t)}{\mathrm{d}t} \tag{109}$$

$V^{\wedge}_{\mathrm{Pe}}(\mathrm{TE})$ can be determined through the time integration of (98) from 0 to TE, according to the following expression:

$$V^{\wedge}_{\mathrm{Pe}}(\mathrm{TE}) = V^{\wedge}_{\mathrm{Pe}}(0) + \int_0^{\mathrm{TE}} \phi^{\wedge}_{\mathrm{EXP}}(t)\mathrm{d}t = C_{\mathrm{P}}P_{\mathrm{GI}} - V^{\wedge}_{\mathrm{TIDe}} \tag{110}$$

The equivalence between the second and the third members of (110) takes into account the relation (102) as well as the definition of expiratory tidal volume ($V^{\wedge}_{\mathrm{TIDe}}$), as follows:

$$V^{\wedge}_{\mathrm{TIDe}} = \int_0^{\mathrm{TE}} \phi^{\wedge}_{\mathrm{EXP}}(t)\mathrm{d}t \tag{111}$$

The detection of $V^{\wedge}_{\mathrm{TIDe}}$ is performed by the ALVS monitoring system through the implementation of (111).

(110) and (111) compared with (95) and (96) take in to account the opposite direction of $\phi^{\wedge}_{\mathrm{EXP}}$ with respect to that of $\phi^{\wedge}_{\mathrm{INS}}$, since $\phi^{\wedge}_{\mathrm{INS}}$ and $\phi^{\wedge}_{\mathrm{EXP}}$ are considered positive and negative quantities, respectively. For this reason, $V^{\wedge}_{\mathrm{TIDe}}$ established by (111) should be considered negative but of an absolute value equal to that of positive $V^{\wedge}_{\mathrm{TIDi}}$ established by (96).

As a global result of a controlled breathing lasting a time equal to the sum $\mathrm{TI}^* + \mathrm{TE}^*$, the following relation should occurs:

$$V^{\wedge *}_{\mathrm{TIDi}} = -V^{\wedge *}_{\mathrm{TIDe}} \tag{112}$$

where $V^{\wedge *}_{\mathrm{TIDe}}$, according to (111), is the tidal volume discharged during an expiration lasting a time equal to TE^*.

R_{EXP} can be obtained from (78) along with (106) or in alternative way from (107).

The waveform of ventilation parameters ($\phi^{\wedge}_{\mathrm{VEN}}$, $\phi^{\wedge}_{\mathrm{EXT}}$, $\phi^{\wedge}_{\mathrm{RES}}$, $V^{\wedge}_{\mathrm{P}}$, $P^{\wedge}_{\mathrm{AW}}$, $P^{\wedge}_{\mathrm{EA}}$) and of ALVS components output (P_{G}, R_{G}, R_{EXT}) for a square waveform as P_{AW} excitation with TI and TE equal to $5\tau^{\wedge}_{\mathrm{INS}}$ and $5\tau^{\wedge}_{\mathrm{EXP}}$, respectively, are reported in the Fig. 7.

The waveforms layout carried out with or without the application of the compensation procedure is represented in the Fig. 7 with continuous or dashed lines.

As it is clear observing the Fig. 7, a real P_{AW} square waveform is obtained by modeling R_{G} waveform during inspiration and expiration times according to (72) and (82), respectively (Section 4.2)

4.4. Tidal or minute volume control in conventional DCV

In conventional DCV the operator at the beginning of assisted/controlled ventilation treatment arbitrarily sets the value of the following parameters: $\mathrm{PEEP}_{\mathrm{EXT}}$ (cm H_2O), FR (acts/min), I:E and V_{TID} or V_{MIN} (l).

FR is the frequency of breathing defined as follows:

$$\mathrm{FR} = \frac{1}{\mathrm{TR}} = \frac{1}{\mathrm{TI} + \mathrm{TE}} \tag{113}$$

where TR is the breathing period equals to the sum TI + TE.

I:E denotes the following a dimensional ratio:

$$I : E = \frac{\mathrm{TI}}{\mathrm{TE}} \tag{114}$$

Once both FR and I:E have been set, from (113) and (114) TI and TE are determined in seconds as follows:

$$\mathrm{TI} = \frac{60(I : E)}{\mathrm{FR}[1 + (I : E)]} \tag{115}$$

$$\mathrm{TE} = \frac{60}{\mathrm{FR}[1 + (I : E)]} \tag{116}$$

V_{MIN} denotes the so-called minute volume, i.e. the volume delivered to the patient for every minute, which is given by the following expression:

$$V_{\mathrm{MIN}} = \mathrm{FR}\,V_{\mathrm{TID}} \tag{117}$$

Thus, in conventional DCV the regulation of both upper (P_{GI}) and lower ($\mathrm{PEEP}_{\mathrm{EXT}}$) P_{AW} levels provides for the control of required V_{TID} or V_{MIN} during pre-established TI and TE.

All that neglects very relevant and critical ventilation parameters as real value assumed by P_{EA} at the end of both inspiration and expiration as well as R_{INS}, R_{EXP} and C_{P}.

4.5. Tidal or minute volume control in advanced DCV

The results obtained in Section 4.3 can be summarized as follows.

The first controlled breathings (about 20 for statistical improvement) must be devoted to diagnostic evaluation, keeping P_{AW} on P_{GI} and $\mathrm{PEEP}_{\mathrm{EXT}}$ values for the time required to the vanishing of $\phi_{\mathrm{INS}}(\mathrm{TI}^*)$ and $\phi_{\mathrm{EXP}}(\mathrm{TE}^*)$, respectively.

In such a way TI^* and TE^* evaluation provides for the determination of both $\tau^{\wedge}_{\mathrm{INS}}$ and $\tau^{\wedge}_{\mathrm{EXP}}$ and hence of optimal TI and TE to be selected as follows:

$$\mathrm{TI} = \mathrm{TI}^* = 5\tau^{\wedge}_{\mathrm{INS}} = 5R_{\mathrm{INS}}C_{\mathrm{P}} \tag{118}$$

$$\mathrm{TE} = \mathrm{TE}^* = 5\tau^{\wedge}_{\mathrm{EXP}} = 5R_{\mathrm{EXP}}C_{\mathrm{P}} \tag{119}$$

$$I : E = \frac{\mathrm{TI}}{\mathrm{TE}} = \frac{R_{\mathrm{INS}}}{R_{\mathrm{EXP}}} \tag{120}$$

$$\mathrm{TR} = \mathrm{TI} + \mathrm{TE} = 5C_{\mathrm{P}}(R_{\mathrm{INS}} + R_{\mathrm{EXP}}) \tag{121}$$

$$\mathrm{FR} = \frac{60}{\mathrm{TR}} = \frac{12}{C_{\mathrm{P}}(R_{\mathrm{INS}} + R_{\mathrm{EXP}})} \tag{122}$$

Of course, the choices $\mathrm{TI} > \mathrm{TI}^*$ and $\mathrm{TE} > \mathrm{TE}^*$ keep all the diagnostic and therapeutic advantages described in Section 4.3, but both determine a reduction of FR with respect to the value established by (122).

So that, (122) provides the high cut-off threshold for FR below which the optimal condition of breathing control is retained.

The monitoring of both ϕ_{INS} and ϕ_{EXP} together with P_{GI} and $\mathrm{PEEP}_{\mathrm{EXT}}$ regulation allow the determination and the automatic control of R_{INS}, R_{EXP}, C_{P} and V_{TID} or V_{MIN}, according to the following expressions:

$$C_{\mathrm{P}} = \frac{V_{\mathrm{TID}}}{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}} \tag{123}$$

$$R_{\mathrm{INS}} = \frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{\phi^{\wedge}_{\mathrm{INS}}(0)} = \frac{\tau^{\wedge}_{\mathrm{INS}}}{C_{\mathrm{P}}} \tag{124}$$

$$R_{\mathrm{EXP}} = \frac{P_{\mathrm{GI}} - \mathrm{PEEP}_{\mathrm{EXT}}}{\phi^{\wedge}_{\mathrm{EXP}}(0)} = \frac{\tau^{\wedge}_{\mathrm{EXP}}}{C_{\mathrm{P}}} \tag{125}$$

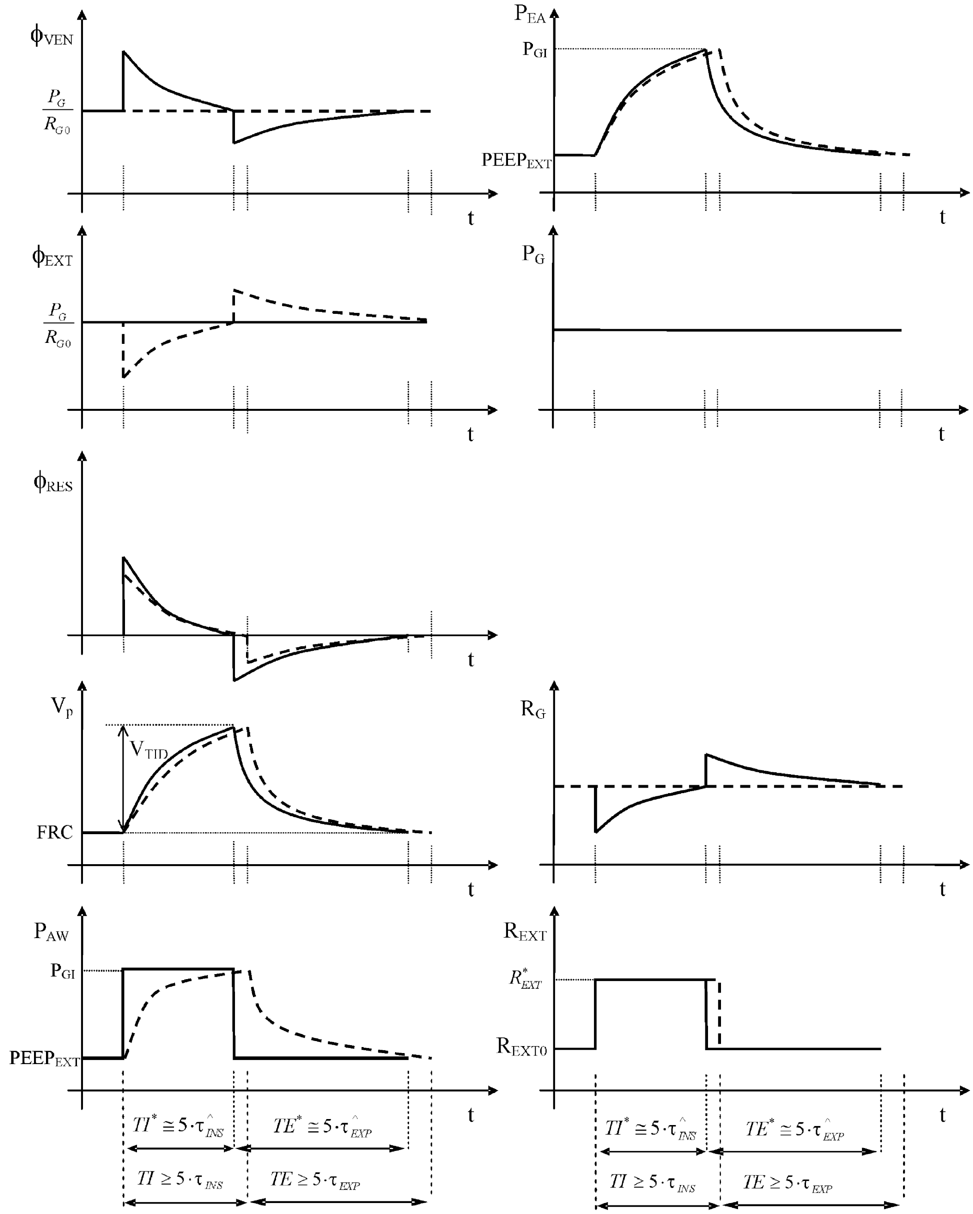

Fig. 7. Time-waveform of ventilation parameters (ϕ_{VEN}; ϕ_{EXT}; ϕ_{RES}; V_P; P_{AW}; P_{EA}) and of ALVS components output (P_G; R_G; R_{EXT}) in advanced dual-controlled ventilation with square waveform as airways pressure (P_{AW}) excitation occurring with (continuous lines) or without (dashed lines) the application of the compensation procedure. See text.

$$V_{TID} = \int_0^{TI} \phi_{\hat{INS}}(t)\mathrm{d}t = C_P(P_{GI} - \mathrm{PEEP}_{EXT}) \tag{126}$$

$$V_{MIN} = \mathrm{FR}V_{TID} = 12\left(\frac{P_{GI} - \mathrm{PEEP}_{EXT}}{R_{INS} + R_{EXP}}\right) \tag{127}$$

(126) and (127) point out that V_{TID} and V_{MIN} are independent on R_P (R_{INS}; R_{EXP}) and C_P, respectively.

5. Experimental results

The functional performance of the following three ALVS components assumes a relevant role for the experimental control of ventilation process:

(a) proportional valve;
(b) respiratory system simulator (DRSS);
(c) monitoring system.

The proportional valve, consisting in an airflow regulator, has been properly designed for simulating the airflow resistance (R_G) of the STFGS. The regulation of the flow level crossing the valve is actuated by the variation of its pipe geometrical configuration. The internal geometry of the pipe can be changed through the displacement of a piston along its longitudinal axis carried out by a stepping motor controller. The longitudinal profile of the piston has been selected in

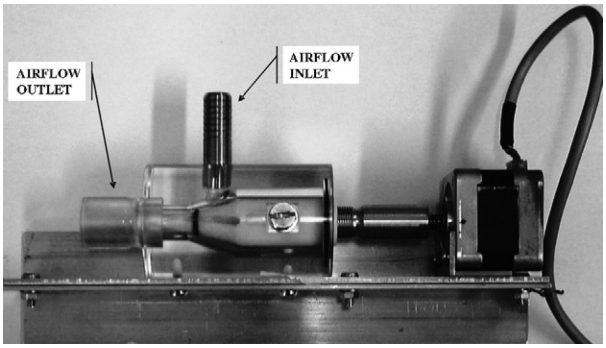

Fig. 8. Picture of the proportional valve included in the ALVS.

order to keep the airflow inside the pipe in accordance with the laminar configuration (Section 4), even with the higher working pressure. The airflow as a function of the piston position is quite linear in the working range from 0.2 to 120 l/min. The sensibility of airflow regulation inside the linear range reaches 1.5 l/min with the working pressure of 500 cm H_2O. These functional features are well suited for stationary control of ventilation process. Moreover, the hystheresis effects lower than 12% as well as the response time to the required piston displacement of the order of 100 ms allow the transient control during the breathing time through the compensation procedure (Section 4.2). The Fig. 8 shows a picture of the proportional valve realized.

The DRSS consists of the LUNG SIMULATOR by SMS Healthcare (UK) connected to a regulation–calibration system properly designed to expand the range of R_P and C_P simulation as well as to calibrate the DRSS in the working condition considering a linear approximation model. As a result, DRSS can simulate the following discrete distribution of airways resistance (R_P) and lung compliance (C_P) values:

(a) $R_P = 0, 5, 10, 20, 50, 100, 200\,\mathrm{cm\,H_2O\,s\,l^{-1}}$ calibrated inside the airflow range 0.1–2 l/s;
(b) $C_P = 10, 20, 25, 50\,\mathrm{ml/cm\,H_2O}$ calibrated inside the FRC and V_{TID} ranges 0–0.1 l and 0.1–1 l, respectively.

The inertia of the DRSS mechanical framework does not allow the reproduction of R_P and C_P transient variation occurring during the breathing time. Nevertheless, DRSS represents an adequate experimental device for studying the steady state condition occurring after any R_P or/and C_P variation. Thus, it exhibits a quite linear V_P–P_{EA} relationship if the value of both FRC and V_{TID} fits the clinical range normally adopted for DCV treatment.

The monitoring system of ALVS includes two pressure sensors Honeywell 40PC Series (±50 mmHg) connected with the DRSS for the measurement of both airways and endoalveolar pressures along with two airflow sensors Honeywell AWM700 Series (0–200 l/min) inserted in the STFGS and TVAPS for the measurement of both ventilation and external airflows. The functional features of both the above-mentioned sensors fit well to the experimental requirements of the present work. In particular, the measurement error affecting the real time monitored pressure and airflow is about 5%.

In order to check the theoretical results obtained in Section 4, a great number of laboratory tests have been performed with ALVS.

The first group of experimental tests, planned for evaluating the solution proposed in Section 4.4, demonstrates that ALVS successfully provides the compensation procedure for advanced DCV with square waveform as P_{AW} excitation if the FR does not exceed the value of about 20 acts/min. This result is consisted with controlled breathing of adult or child patient.

The second group of experimental tests was devoted to the attempt of the optimal control of breathing and the theoretical results carried out in Section 4.3. To the purpose, the DRSS was initially set for simulating a typical healthy adult patient with the following characteristics and requirements:

$$R_{INS} = 10\,\mathrm{cm\,H_2O\,s\,l^{-1}}, \qquad R_{EXP} = 20\,\mathrm{cm\,H_2O\,s\,l^{-1}},$$
$$C_P = 25\,\mathrm{ml/cm\,H_2O}, \qquad \mathrm{FRC} = 50\,\mathrm{ml}$$

The error affecting the simulation of R_P and C_P values is about 10 and 15%, respectively.

According to (88) and (118)–(122), on account of the reported experimental error the following results have been detected:

$$\mathrm{PEEP_{EXT}} = 2.1\,\mathrm{cm\,H_2O}, \qquad \hat{\tau}_{INS} = 0.24\,\mathrm{s},$$
$$\hat{\tau}_{EXP} = 0.51\,\mathrm{s}, \qquad \mathrm{TI} = 1.20\,\mathrm{s}, \qquad \mathrm{TE} = 2.55\,\mathrm{s},$$
$$I : E = 1 : 2.125, \qquad \mathrm{TR} = 3.75\,\mathrm{s}, \qquad \mathrm{FR} = 16\,\mathrm{acts/\min}$$

The *I*:*E* and maximum FR values are both well suited for controlled breathing of adult patient.

Moreover, according to (127), a value of $P_{GI} = 17.5\,\mathrm{cm\,H_2O}$ ensuring the required V_{MIN} of 6.00 l has been monitored.

Thus, according to both (126) and (127), $V_{TID} = 0.38$ l has been obtained.

According to (122), (126) and (127), for a given P_{GI} (17.5 cm H_2O), C_P variations occurring during the ventilation treatment modify both FR and V_{TID} but do not affect V_{MIN}. In order to check such theoretical result, C_P has been changed assuming the value of 20 or 30 ml/cm H_2O. Such changes account for a slight restrictive process or increased lung elastance, respectively. According to the theory developed (Section 4) and to the available DRSS only the steady state after the R_P or C_P changes is considered. With the same V_{MIN} of 6.00 l, FR becomes 20 or 13 acts/min while V_{TID} becomes 0.30 or 0.46 l, respectively.

Otherwise, R_{INS} or/and R_{EXP} variations do not affect V_{TID} but modify V_{MIN}, on account of FR changing. In order to check such theoretical result, R_{INS} and R_{EXP} have been changed assuming the value of 15 or 5 cm $H_2O\,s\,l^{-1}$ and of

25 or 15 cm H_2O s l^{-1}, respectively. Such changes account for a significant obstructive process or decreased airways resistance. With the same V_{TID} of 0.38 l, FR becomes 12 or 24 acts/min while V_{MIN} becomes 4.58 or 9.10 l, respectively.

In the last case, in order to keep the same V_{MIN} of 6.00 l and FRC of 16 act/min with unchanged V_{MIN} of 0.30 l, according to (127), the adjustment of P_{GI} on 22.0 and 12.3 cm H_2O has been required, respectively.

Finally, if the control of V_{TID} is required apart from V_{MIN}, (126) has to be considered and FR can be reduced to more advisable value maintaining the same optimal condition of breathing. As a matter of fact, the value of P_{GI} ensuring the required V_{TID} of 0.50 l has been monitored as follows:

$$P_{GI} = 22.2\,\mathrm{cm\,H_2O}$$

and the reduction of FR below the cut-off value of 16 acts/min has retained the same condition of breathing.

6. Conclusions

The design guidelines of an advanced lung-ventilator system (ALVS) have been carried out in order to reach the following improvements over conventional assisted/controlled ventilation:

(a) dual-controlled ventilation (DCV) optimization with square waveform as airways pressure excitation in anaesthetized or severely brain injured patient for which a linear respiratory mechanics is considered;
(b) adaptive loop control of DCV which accounts the current respiratory characteristics of patient and his diagnostic evaluations both obtained from advanced monitoring system instead of arbitrary pre-established parameters setting;
(c) more realistic approximation of the airways pressure waveform to physiological transpulmonary pressure waveform;
(d) implementation of a compensation procedure developed to let the selected airways pressure waveform become stable and insensitive from the patient's respiratory characteristics.

The experimental results obtained with a versatile lung simulator agree with the theoretical ones and show that ALVS performs the optimization of DCV control when steady condition as well as linear respiratory mechanics are considered. This is useful for the research activity aiming at the improvement of both diagnostic evaluation and therapeutic outcome relative to mechanical ventilation treatments.

In particular, the experimental tests show that it provides the functional features described hereafter.

Through the implementation of a compensation procedure which stabilizes the flow across the resistance controlling the airways pressure applied to the patient, ALVS behaves like an ideal pressure generator. This makes possible any airways pressure waveform of clinical interest during both inspiration and expiration through an identical shape of such resistance waveform, eliminating the dependence of load (respiratory system parameters) fluctuations or variations.

The optimization of breathing control in DCV with square waveform as airways pressure excitation, is carried out setting the time of inspiration and expiration at about five times the inspiratory and expiratory time constant, respectively. In this case, concerning the lung volume control, the according experimental and theoretical results point out that the tidal or minute volume are independent on airways resistance or lung compliance, respectively.

The last results are very interesting for clinical application because an increase of airways resistance (obstructive process) or a reduction of lung compliance (restrictive process) does not affect the control of tidal or minute volume, respectively.

The setting of the optimal time of both inspiration and expiration is implemented through a diagnostic procedure performed real-time by the ALVS monitoring system providing also the waveform of pressure (airways and endoalveolar), respiratory flow and lung volume as a function of time together with the lung volume-airways (endoalveolar) pressure and respiratory flow-lung volume loops, as well as the current value of inspiratory and expiratory airways resistance, static and dynamic lung compliance and respiratory work.

The presence of a continuous flow inside the ventilation circuit allows the compatibility of spontaneous breathing activity of patient by flow or pressure support ventilation with assisted/controlled breathing or/and triggered ventilation.

The favourable results of the present work establish the rationale for clinical test employing advanced DCV with square waveform as airways pressure excitation and suggest new theoretical, experimental and clinical studies in the field of assisted/controlled ventilation with more physiological waveforms as airways pressure excitation. Moreover, non-linearity effects on respiratory mechanics should be investigated in order to expand the application of the proposed approach to a wider range of patient treated with DCV or with assisted ventilation modalities including spontaneous breathing activity.

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