Pressure-flow breath representation eases asynchrony identification in mechanically ventilated patients

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Abstract
Breathing asynchronies are mismatches between the requests of mechanically ventilated subjects and the support provided by mechanical ventilators. The most widespread technique in identifying these pathological conditions is the visual analysis of the intra-tracheal pressure and flow time-trends. This work considers a recently introduced pressure-flow representation technique and investigates whether it can help nurses in the early detection of anomalies that can represent asynchronies. Twenty subjects—ten Intensive Care Unit (ICU) nurses and ten persons inexperienced in medical practice—were asked to find asynchronies in 200 breaths pre-labeled by three experts. The new representation increases significantly the detection capability of the subjects—average sensitivity soared from 0.622 to 0.905—while decreasing the classification time—from 1107.0 to 567.1 s on average—at the price of a not statistically significant rise in the number of wrong identifications—specificity average descended from 0.589 to 0.52. Moreover, the differences in experience between the nurse group and the inexperienced group do not affect the sensitivity, specificity, or classification times. The pressure-flow diagram significantly increases sensitivity and decreases the response time of early asynchrony detection performed by nurses. Moreover, the data suggest that operator experience does not affect the identification results. This outcome leads us to believe that, in emergency contexts with a shortage of nurses, intensive care nurses can be supplemented, for the sole identification of possible respiratory asynchronies, by inexperienced staff.

Keywords Respiratory asynchronies · Mechanical ventilator · ICU monitoring · Breath representation

1 Introduction

In ventilator-assisted patient breathing, asynchronies occur when there is a mismatch between the patient's demand and the support provided by the ventilator in terms of duration, volume, or flow. It is a common problem in ventilated patients and it may cause severe discomfort for patients, compromise ventilator efficacy in decreasing *Work Of Breath* (WOB), and even damage the diaphragm [1–17]. It is therefore a paramount task to detect asynchronies and intervene promptly.

Modern mechanical ventilators can sample patients' airways pressure, flow, and volume hundreds of times per second, and represent them as waveforms on a device monitor. The waveform-based representation of respiratory acts grants the specialist some knowledge of the patient-ventilator interaction, and it also provides a valuable tool to detect many ventilation conditions such as asynchronies. Nevertheless, manual waveform analysis is a complex task requiring specific competency that only a few specialists can achieve.

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Because of this, many issues concerning patient-ventilator interaction are often under-diagnosed, with negative consequences for patients who, receiving inappropriate ventilation support, undergo a worsening of autonomous respiratory activities and an increased mortality risk [16].

Another method for detecting asynchronies is the monitoring of the oesophageal pressure waveform. The main limitations are that it is semi-invasive, requires strict calibration, and the accuracy of the signal is affected by several variables (e.g., patient's posture, cardiac activity, swallowing, position, and volume of inflation of the oesophageal balloon); moreover, specific skills for the interpretation of tracings are required [18, 19]. As an alternative one can use the *Neurally Adjusted Ventilatory Assist* (NAVA®), which requires a nasogastric catheter for the detection of the *Electrical Activity of the Diaphragm* (EAdi) [20], but also this technique is semi-invasive. Moreover, patients can trigger ventilators by using solely the auxiliary respiratory muscles; this means, according to the "first-come, first-served" principle, that even during NAVA® there may be a spontaneous ventilatory activity, and therefore asynchrony, even in the absence of any EAdi evidence. In fact, in this specific case, the software switches to an actual *Pressure Support Ventilation* (PSV) with a non-diaphragmatic pneumatic trigger [21–23].

In general, a fundamental aspect of managing the problem of asynchronies is the collaboration between physicians and nurses. Among the other activities, nurses provide an important shortcut bridge between patients and clinicians in ICU. Since they are usually more strictly in contact with patients than clinicians, nurses may help the latter in obtaining a more rapid response to abnormal breathing activities. In this context, easy identification of possible asynchronies to request an expert diagnosis is crucial for early responses. Note that Chacon *et al.* proved that after specific training of two hours a day for twenty days, based on the observation of flow and pressure waveforms, ICU nurses were able to detect *Ineffective Efforts during Expiration* (IEE) as well as expert physicians [24]. However, the focus was only on IEE, and other types of asynchrony were not considered.

Recently, a new asynchrony identification approach, based on the analysis of the breath representation in the pressure-flow space, has been patented [25] and proposed to replace the usual pressure-time and flow-time portrayal [26]. Since this technique would require a hardware upgrade of the ventilation machinery, which may not always be possible in the current generation of ventilators, this work has two aims: on the one hand, it appraises the efficiency difference between the new approach and the standard one in ahead identification of possible asynchronies performed by humans; on the other hand, it gauges the importance of the operator's experience in the identification process.

To achieve these goals, a group of three experts in the field labeled one by one 200 breaths as either "containing at least one asynchrony" or "not containing any asynchrony", with no distinction between inspiratory, expiratory, or cycling-off asynchronies. Then, we measured the sensitivities, specificities, and evaluation times of 20 individuals—10 ICU nurses and 10 inexperienced subjects with no medical practice—in asynchrony identification on the pre-labeled breaths, comparing the new approach with the classical one.

As far as the first goal, this work compares the results due to the adopted identification technique on the whole set of subjects, on the nurses, and the inexperienced group, and the Wilcoxon signed-ranks test [27] establishes whether there exists any statistically significant difference in using one of the two identification techniques in place of the other.

About the importance of the experience in early asynchrony identification, the Mann–Whitney U test [28] is applied to both compare nurse and inexperienced groups on each classification technique and discover whether the experience impacts the subjects' sensitivities, specificities, or classification times in any of the two approaches.

2 Materials and methods

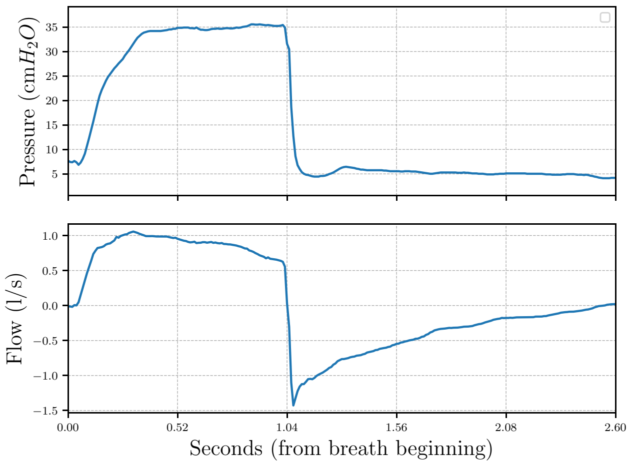
2.1 Loop-based characterization of asynchronies

Mechanical ventilator usually represents respiratory acts as two plots depicting both patients' pressure and airflow over time, such as those reported in Fig. 1.

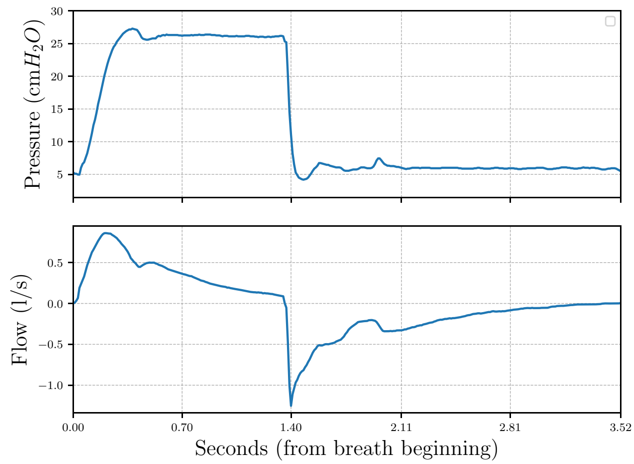
Even if it is theoretically possible to distinguish between a normal breath without asynchronies (see Fig. 1a) and a pathological breath with one or more asynchronies (Fig. 1b), in practice the task is quite arduous; indeed it is necessary to train nurses following a specific protocol [24], since the differences between the normal and the pathological case are not always so clear.

The breath's pressure-flow representation consists of a curve that produces a sort of an elliptic cycle, such as that depicted in Fig. 2a. In normal conditions, both pressure and flow rise during the first part of the inspiration. Then, the flow reaches the maximum and declines down to 0. As soon as the flow becomes negative, the expiration begins, the pressure decreases, and its trend stands still until the end of the breath. From a physical perspective, the area in this pressure-flow curve corresponds to the power (P) expressed during the breath cycle in terms of airflow and pressure, and WOB equals $P * \delta t$, where δt is the time elapsed during the breath.

Any *Sub-Breath Loops* (SBLs), decorating the primary curve, represents a work overload which is measurable by computing its area and which, according to [26], may denote a ventilation asynchrony. Figure 2b contains two SBLs: the

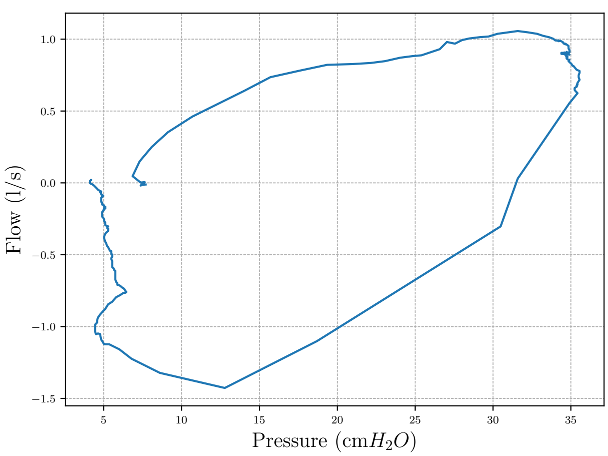


(a) The pressure-time and flow-time representation of a breath that, according to the majority of the experts, does not contain asynchronies

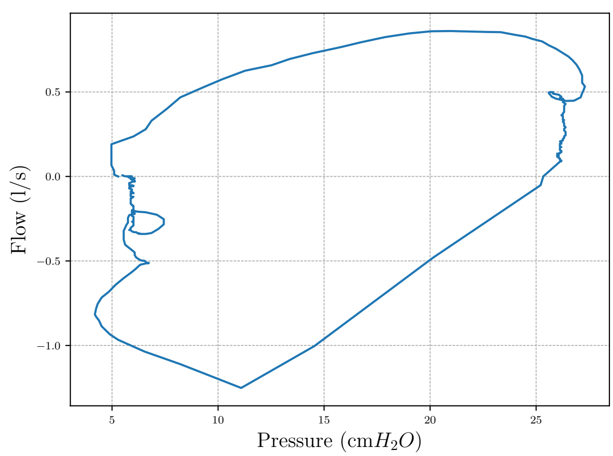


(b) The pressure-time and flow-time representation of a breath that, according to the majority of the experts, does contain asynchronies

Fig. 1 The pressure-time and flow-time representation of two breaths



(a) The pressure-flow representation of a breath is depicted as time-domain waveforms in Fig. 1a. According to the majority of the experts, it does not contain asynchronies



(b) The pressure-flow representation of a breath is depicted as time-domain waveforms in Fig. 1b. According to the majority of the experts, this breath does contain asynchronies

Fig. 2 The pressure-flow representation of the two breaths depicted as time-domain waveforms in Fig. 1

small one, whose samples have pressure above 25 cm H_2O and flow between 0 and 0.5 l/s, occurs during the inspiratory phase; the larger one, whose pressure and flow are between 5 and 10 cm H_2O and between -0.5 and 0, respectively, appears during the expiratory phase.

2.2 Data-set extraction and labeling

As far as the breath data, we retrospectively analyzed data used in a previously published study [26].

Airway flow (f), pressure (p), and EAdi samples for a total of 50228 breaths by eight critically ill mechanically ventilated patients were considered. The patients were ventilated with Servo-I® (Maquet) in different modalities: *Pressure Regulated Volume Controlled* (PRVC), *Pressure Support* (PS), *Synchronized Intermittent Mandatory Ventilation-Volume Controlled* (SIMV-VC), *Synchronized Intermittent Mandatory Ventilation-Pressure Controlled* (SIMV-PC), *Volume Control* (VC), *Volume Support* (VS) and *Neurally Adjusted Ventilatory Assist* (NAVA®).

2.2.1 Data-set selection

We produced the pressure-time, the flow-time and the EAdi-time plots of all the 50228 breaths in the data set. By observing these plots, we preliminarily selected 202 breaths so that, according to our initial coarse evaluation, the number of respiratory acts that seemed to contain asynchronies was about the same as those that appeared to be normal. We admitted asynchronies in any breath cycle phases, being in either inspiration, cycling, or expiration.

2.2.2 Data-set labeling by expert

The flow-time, pressure-time, and EAdi-time plots of the selected 202 breaths were analyzed by three ICU expert physicians that individually labeled each of the respiratory acts as "containing asynchronies" or "non-containing asynchronies". Finally, the consensus between the evaluations of the experts was produced by a majority. According to it, 97 breaths among the 202 contained asynchronies and the remaining 105 were normal acts.

2.3 Testing the SBL-based identification of asynchronies

2.3.1 Breath representations

Each of the 202 selected breaths was depicted by two distinct images: an image representing both the pressure-time and the flow-time plots, such as those reported in Fig. 1, and an image reporting the pressure-flow plot of the breath itself, see Fig. 2 for two examples. We call "*waveform breath representation*" the former images and "*pressure-flow breath representation*" the latter.

It is worth noticing that the EAdi-time plots were employed by the experts to produce the consensus, while they have not been used during the following classification phase of the experiment.

2.3.2 Classifier selection and training

We considered 20 individuals. Half of them were nurses with at least three years of working experience at the general and post-operative ICU of the Cattinara University Hospital, Trieste, Italy, whose average age and standard deviation are about 43.3 and 10.49; this group is called "nurse group". The remaining subjects—i.e., 10 individuals whose average age and standard deviation are about 43.2 and 19.27, respectively—were not involved in medical practices, they had never seen any waveform and pressure-flow representations of a breath before the experiment, and they knew neither the source nor the meaning of these plots. This group is named the "inexperienced group".

Among the 202 classified breaths, we randomly selected one representative for the breaths that, according to the expert consensus, do not contain any asynchrony, and one for those having asynchrony. We used exactly the breath associated with Figs. 1a and 2a as an example of the case without asynchronies, and the breath associated with Figs. 1b and 2b as an example of the case containing asynchronies. These two breaths and their respective representations were used to train the considered individuals about asynchrony identification.

Because of their job, all the subjects in the nurse group were assumed to know normal activity in waveform breath representation in the time domain. Figure 2a and b were instead shown as examples of the pressure-flow breath representation and the SBLs in Fig. 2b were pointed out as clues for asynchronies. This activity took about one minute and was the only training that the nurse group had in distinguishing asynchronies from normal activity in pressure-flow breath representation.

While the nurses were physically located in the same place during the training session, the components of the inexperienced group came from different geographical areas and, because of this, they were trained on-line by using a video. Figures 1 and 2 were used as examples for the two kinds of images to consider: Figures 1a and 2a were presented as "normal" images, while Figs. 1b and 2b were exhibited as "abnormal" images. In particular, the bumps in Fig. 1b around 0.35 s and 1.85 s, and the SBLs in Fig. 2b were highlighted as unwanted and to-be-reported events.

2.3.3 Subjects' evaluation

The subjects were asked to individually evaluate the 200 breaths in the consensus not used for the training. The evaluations were repeated twice: first, by using the waveform representation of the breaths (*waveform-based classification*) and, then, by analyzing their pressure-flow representations (*SBL-based classification*). During both rounds, the image order was shuffled so to avoid memory-based bias. A dedicated web application collected the subject classifications and recorded the elapsed time. The subjects were also asked for permission to store and publish their ages and professions

Table 1 The subjects considered by this study

ID	Age	Profession	ID	Age	Profession
1	41	ICU Nurse	11	31	Musician
2	28	ICU Nurse	12	31	Teacher
3	63	ICU Nurse	13	63	Retired
4	50	ICU Nurse	14	47	Univ. Associate Professor
5	51	ICU Nurse	15	24	Univ. Student
6	47	ICU Nurse	16	59	School Manager
7	41	ICU Nurse	17	18	High School Student
8	43	ICU Nurse	18	65	Retired
9	28	ICU Nurse	19	26	Univ. Student
10	41	ICU Nurse	20	68	Retired
(a) The nurse group.			(b) The inexperienced group.		

They were asked for permission to store and publish their ages and professions for statistical purposes only and they all agreed

for statistical purposes only, and they all agreed (see Table 1 for the data).

Each of the nurses was asked to establish, for each of the breaths, whether it contained at least one asynchrony during the waveform-based classification and to indicate the presence of SBLs decorating the complete breath loop cycles in the SBL-based classification.

The components of the inexperienced group were instead asked to identify bumps present in both of the two plots, i.e., the pressure-time and flow-time waveforms, during the waveform-based classification, and to signal the presence of SBLs in the pressure-flow breath representation.

2.4 Statistical analysis

The consensus between the experts was considered as the standard of reference against which subjects' evaluations were compared. For each of the subjects and each of the waveform-based and SBL-based classification rounds, we built a confusion matrix which reported the number of true positives (TP)—i.e., the evaluations which were consistent with the consensus and classified a breath as containing at least one asynchrony-, true negatives (TN)—i.e., the evaluations which were consistent with the consensus and classified a breath as not containing any asynchrony-, false positives (FP)—i.e., the evaluations which, differently from the consensus, classified a breath as containing at least one asynchrony-, and false negatives (FN)—i.e., the evaluations which does not agree with the consensus, classified a breath as not containing any asynchrony (see Table 2). Then, we computed the sensitivity (SE) and specificity (SP) of each of the confusion matrices as follows

$$\mathrm{SE} \stackrel{\mathrm{def}}{=} \frac{\mathrm{TP}}{\mathrm{TP}+\mathrm{FN}} \qquad \mathrm{SP} \stackrel{\mathrm{def}}{=} \frac{\mathrm{TN}}{\mathrm{TN}+\mathrm{FP}} \tag{1}$$

Sensitivity, specificity, and total classification time data were individually considered (see Table 3 and Figs. 3, 4, and 5) and the two-tailed Wilcoxon signed-ranks test [27] was applied to establish whether subjects' performances were improved by using the SBL-based classification in place of the waveform-based classification (*overall analysis*). We selected as threshold p-value 0.05 to discharge the null hypothesis that "the medians of the data associated to the waveform-based and SBL-based classifications are the same". The W-value was computed and compared with the critical value due to the p-value threshold and the number of uneven paired samples. The same statistical tests were also internally applied to each of the considered groups: the *nurse analysis* dealt with the differences between waveform-based and SBL-based classifications performed by the nurses; the *inexperienced analysis* investigated the effects of these two approaches on the performances of the inexperienced subjects.

Furthermore, the two-tailed Mann–Whitney U test [28] was applied to compare nurse and inexperienced groups on each classification technique and to discover, by using once more as p-value 0.05, whether the experience impacts the sensitivity, the specificity, or the classification time of the subjects (*waveform analysis* and *SBL analysis*). For both waveform and SBL analysis, we computed the U-value and compared it with the critical value associated with both the p-value threshold and the number of considered subjects. The mean values of all the considered data distributions were also evaluated, to establish an order among the means themselves whenever the null hypothesis was discharged.

Table 2 The number of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) cases concerning the consensus by a majority among the experts per subject

		Waveforms					SBLs				
Group	Id	TP	FP	FN	TN	Time	TP	FP	FN	TN	Time
Nurse	1	82	50	14	54	578	84	41	12	63	553
	2	72	38	24	66	1208	84	50	12	54	425
	3	41	16	55	88	584	86	45	10	59	456
	4	68	60	28	44	1025	90	53	6	51	700
	5	40	38	56	66	768	92	54	4	50	798
	6	22	14	74	90	1378	87	49	9	55	661
	7	48	40	48	64	664	89	56	7	48	661
	8	68	71	28	33	1213	88	49	8	55	543
	9	74	42	22	62	815	85	44	11	60	530
	10	80	60	16	44	942	87	52	9	52	461
Inexp.	11	65	39	31	65	1747	88	48	8	56	826
	12	67	43	29	61	906	87	48	9	56	433
	13	76	49	20	55	642	86	53	10	51	893
	14	35	20	61	84	1326	90	55	6	49	485
	15	23	21	73	83	761	84	48	12	56	315
	16	64	57	32	47	2506	88	49	8	55	545
	17	79	74	17	30	1043	84	50	12	54	479
	18	70	44	26	60	1746	86	59	10	45	553
	19	48	28	48	76	837	85	47	11	57	484
	20	72	50	24	54	1450	87	49	9	55	541

The table reports these data for both waveform-based and SBL-based classifications. The reported classification times are expressed in seconds and refer to the total amount of time required to classify all the exhibited images

Table 3 The sensitivity (SE), specificity (SP), and total evaluation time in seconds (Time) of each subject in both waveform-based and SBL-based classifications

		Waveforms			SBLs		
Group	Id	SE	SP	Time	SE	SP	Time
Nurse	1	0.85	0.52	578	0.88	0.61	553
	2	0.75	0.63	1208	0.88	0.52	425
	3	0.43	0.85	584	0.90	0.57	456
	4	0.71	0.42	1025	0.94	0.49	700
	5	0.42	0.63	768	0.96	0.48	798
	6	0.23	0.87	1378	0.91	0.53	661
	7	0.50	0.62	664	0.93	0.46	661
	8	0.71	0.32	1213	0.92	0.53	543
	9	0.77	0.60	815	0.89	0.58	530
	10	0.83	0.42	942	0.91	0.50	461
Inexp.	11	0.68	0.63	1747	0.92	0.54	826
	12	0.70	0.59	906	0.91	0.54	433
	13	0.79	0.53	642	0.90	0.49	893
	14	0.36	0.81	1326	0.94	0.47	485
	15	0.24	0.80	761	0.88	0.54	315
	16	0.67	0.45	2506	0.92	0.53	545
	17	0.82	0.29	1043	0.88	0.52	479
	18	0.73	0.58	1746	0.90	0.43	553
	19	0.50	0.73	837	0.89	0.55	484
	20	0.75	0.52	1450	0.91	0.53	541

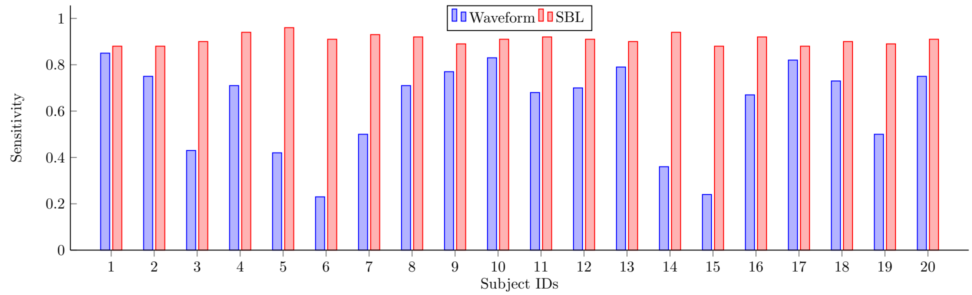


Fig. 3 Sensitivities of the subjects (higher is better). The subjects from 1 up to 10 belong to the nurse group and the remaining ones, i.e., from 11 to 20, to the inexperienced group

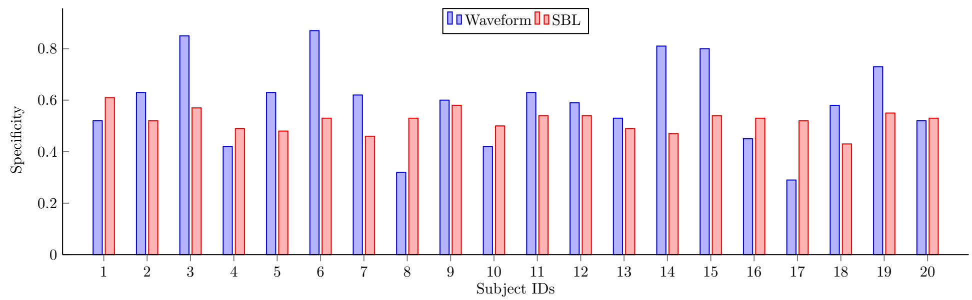


Fig. 4 Specificities of the subjects (higher is better). The subjects from 1 up to 10 belong to the nurse group and the remaining ones, i.e., from 11 to 20, to the inexperienced group

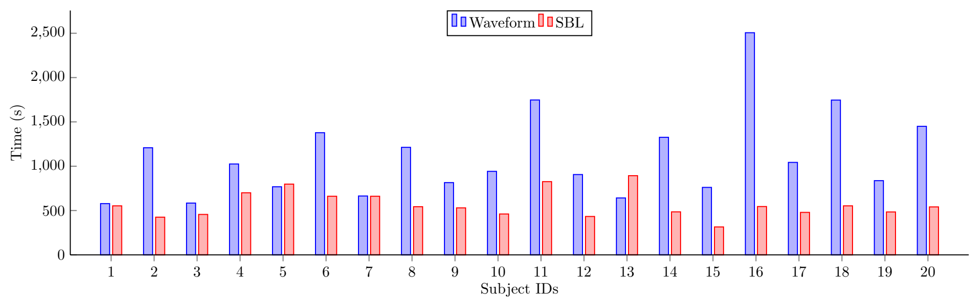


Fig. 5 Classification times in seconds per subject (lower is better). The subjects from 1 up to 10 belong to the nurse group and the remaining ones, i.e., from 11 to 20, to the inexperienced group

Table 4 The average sensitivity (SE), specificity (SP), and classification time in seconds (Time) for both waveform-based and SBL-based classifications for all the subjects (Overall), the nurse group, and the inexperienced group

Index avg.	Overall		Nurse group		Inexp. group	
	Waveform	SBL	Waveform	SBL	Waveform	SBL
SE	0.622	0.905	0.620	0.908	0.624	0.901
SP	0.589	0.520	0.588	0.526	0.591	0.513
Time	1107.0	567.1	917.5	578.8	1296.4	555.4

3 Results

The consensus accounted for 97 breaths labeled as "containing asynchronies" (such as ineffective efforts during expiration (IEEs), flow asynchronies, or delayed-termination asynchronies) and 105 breaths labeled as "non-containing asynchronies". One breath in the former group and one in the latter were used to train the subjects; thus, each individual was requested to classify 200 breaths twice (96 containing at least one asynchrony and 104 not containing asynchronies): once during the waveform-based classification and once during the SBL-based classification.

Table 2 reports the confusion matrix and the overall classification time associated with each subject for waveform-based and SBL-based classifications. Table 3 presents the sensitivity and specificity of each subject in both waveform-based and SBL-based classifications, along with the required classification time. Figures 3, 4, and 5 graphically summarize the data contained in Table 3. Table 4

Table 5 Wilcoxon signed-ranks test results for waveform-based versus SBL-based classifications on the overall subjects (first column), on the nurse group (second column), and the inexperienced group (third column) and Mann–Whitney U test results for nurse group versus inexperienced group on both waveform-based and SBL-based classifications (fourth and fifth columns, respectively)

	Overall W-values	Nurse W-values	Inexp. W-values	Waveform U-values	SBL U-values
Sensitivity	0 (52)	0 (8)	0 (8)	*46* (23)	*43* (23)
Specificity	*58.5* (52)	*17* (8)	*13* (8)	*49.5* (23)	*48* (23)
Time	8 (52)	3 (8)	1 (8)	*29* (23)	*44.5* (23)

Each column reports either the W-values (first column, second, and third) or the U-values (fourth and fifth columns) for sensitivity, specificity, and overall classification time comparisons. The number between parenthesis is the critical value for the specific test. The content of a cell was italicized only when the corresponding test failed to discharge the null hypothesis

contains the average values of all the analyses and all the classification rounds. Table 5 consists of the W-values for the overall, nurse, and inexperienced group analyses and the U-values for both waveform and SBL analyses of the sensitivity, specificity, and classification time data. The numbers between parentheses are the critical value associated with the threshold p-value 0.05 for the specific samples. The null hypothesis is rejected when the W-value (the U-value) is smaller than the corresponding critical value. Please, notice that the critical values for the Wilcoxon signed-ranks test (first three columns in Table 5) changed according to the number of uneven values in the considered paired samples.

The W-value of the overall analysis about sensitivity is 0 and, since it is smaller than the corresponding critical value—i.e., 52-, the null hypothesis was discharged. Thus, we can state that the sensitivities of the overall group improved after switching from the waveform-based classification, whose average was 0.622, to the SBL-based approach, whose average was 0.905. The same situation also holds for both nurse and inexperienced group analyses: since the W-value and the critical value are 0 and 8, respectively, in both the cases, the sensitivity of both the nurse group and the inexperienced group significantly increases by switching from the waveform-based to the SBL-based classification. The former raises its average sensitivity from 0.620 to 0.908 and the latter from 0.624 to 0.901. On the contrary, the U-values of waveform and SBL analyses about sensitivity are 46 and 43, respectively, and, since the critical value is 23 in both cases, the null hypothesis "the experience differences between nurse and inexperienced groups did not affect the sensitivity", cannot be discharged.

Dealing with the specificity, neither the W-values of the overall analysis—i.e., 58.5-, the nurse analysis—i.e., 17-, and the inexperienced analysis—i.e., 18—nor the U-values of waveform and SBL analyses—i.e., 49.5 and 48, respectively—are smaller than the corresponding critical values—i.e., 52, 8, 8, 23, and 23, respectively. Thus, despite a mild decrease in average specificity values (see Table 4, second row), we could not exclude that this contraction was due to the chance.

The W-value associated with the classification times together with the corresponding average values suggested that the use of SBL-based classification in place of the waveform-based one sped up the breath classifications of the overall group and lowered its average time from more than 18 min ($1107.0/60 \approx 18.45$ min) to less than 10 min ($567.1/60 \approx 9.45$ min). The very same situation also internally holds in both the nurse group (W-value and critical value are 3 and 8, respectively) and the inexperienced group (W-value and critical value are 1 and 8, respectively) and, by switching from the waveform-based classification to the SBL-based, their average classification times decreased from more than 15 min ($917.5/60 \approx 15.29$ min) to less than 10 min ($578.8/60 \approx 9.65$) and from more than 21 min ($1296.4/60 \approx 21.61$ min) to less than 10 min ($555.4/60 \approx 9.26$), respectively. Finally, the Mann–Whitney U test could not certify a meaningful difference between the nurse and the inexperienced groups in the evaluation times due to none of the classification approaches. Indeed, the U-values of both waveform-based and SBL-based classifications were greater than the corresponding critical values: 29 and 23 are the U-value and the critical value, respectively, for the former, while 44.5 and 23 are the U-value and the critical value, respectively, for the latter. In a sense, this surprising result certifies the hardness of the asynchrony detection task and the necessity of a specific training, such as that described in [24], even for experienced nurses.

4 Discussion

The discovered upsurge in sensitivity is a substantial result because it allows early asynchrony detection and may avoid severe consequences to mechanically ventilated patients. On the contrary, the moderate specificity contraction we found, for more not statistically significant, is in any case not particularly harmful from the patients' point of view, as it results in specialist evaluations when not strictly necessary.

Also, the speed-up obtained by the classification time is quite significant, since the SBL-based method substantially halves this time, allowing a more user-friendly approach while detecting the closed-loop pattern characterizing a possible asynchrony.

What appears to be unexpected is the fact that inexperienced subjects substantially performed as well as experienced nurses, and this for both the waveform-based and the SBL-based classifications. While for the waveform-based method we can assume that this is an indirect proof of the hardness of the asynchronies detection task, as far as the SBL-based method it sounds like a paramount result: the closed-loop pattern is easily detected by whoever.

As for the clinical meaning of the obtained results, we have to say that pondering the SBL-based detection performed by nurses as a replacement for clinical diagnosis is not a scope of this work, and in any case, the low specificity exhibited by the examined subjects would preclude further step in this direction. SBLs are only an intuitive new graphic breathing representation, which provides more information to clinicians to make decisions. Its application in an ICU could be an important nursing tool to easily recognize anomalies that can represent asynchronies, favoring an early intervention of the clinician. Moreover, SBL-based identification appears to outperform the standard method as an early discovery technique in a more structured–and common—diagnostic framework, where a clinical evaluation follows every warning.

Another important issue, not discussed in this work, is the kind of asynchronies that could be detected, i.e. ineffective efforts, double cycling, reverse triggering, and inspiratory airflow dyssynchrony [29]. But the possibility of distinguishing among specific kinds of asynchronies in the pressure-flow space is a critical topic, and it is still under investigation; so, the SBL-based identification method could prevent proper treatment of these different phenomena. Notice, however, that this issue is not relevant in our settings, since the only thing that matters here is detecting any anomaly in the breathing cycle. This means that the lack of classification for the asynchronies and the moderate absolute specificity, which produces some useless alarms, have little relevance in such a context, since the final diagnosis is always due to the experts. Vice versa, alerting the experts for the vast majority of the real asynchronies is certainly a requested feature in the investigated settings, and the high measured sensitivity accomplishes this task.

Because of the above reasons, it seems reasonable to suggest the switch from wave-form-based to SBL-based early identification of possible asynchronies.

5 Conclusions

We considered 20 subjects: half of them were nurses and the remaining were inexperienced in medical practices. We required all of them to individually blindly classify 200 pre-labeled breaths by using the standard waveform-based classification approach and the new SBL-based classification techniques, with the intent of identifying those breaths which exhibited mechanical ventilation asynchronies.

The average sensitivities over the 20 considered subjects for waveform-based and SBL-based classifications were 0.622 and 0.905, respectively; the specificities were 0.589 and 0.52, respectively; as far as the classification times may concern, their averages were 1107.0 and 567.1 seconds, respectively.

The collected data were analyzed by using the two-tailed Wilcoxon signed-ranks test with a p-value of 0.05 to highlight sensitivity, specificity, and classification time differences between the two approaches in the overall groups and internally to both the nurse group and the inexperienced group. This test highlighted that switching from the waveform-based classifications to the SBL-based classifications increased sensitivity and decreased classification times. Even though the approach change caused a slight contraction in specificity, the Wilcoxon test did not exclude that this was due to the case. The two-tailed Mann–Whitney U test with a p-value of 0.05 was also used to see whether the differences in experience between the nurse group and the inexperienced group affected the sensitivity, the specificity, or the classification times in either waveform-based or SBL-based classifications. According to the collected data and the statistical test, this does not seem to be the case.

The above results suggest that the SBL-based classification can be used instead of the standard waveform-based classification to significantly enhance the early detection of anomalies that can represent asynchronies, both by experienced and inexperienced subjects. Moreover, quite surprisingly, the effectiveness of both the classification approaches seems to be unrelated to the evaluators' experience. Thus, while a specialistic review remains required to establish a diagnosis, in emergency contexts in which there is a shortage of nurses experienced in mechanical ventilation—for example, those due to the COVID-19 pandemic (e.g., see [30–33])-, ICU nurses could be supplemented by inexperienced staff for the sole role of early identification of anomalies which can represent respiratory asynchronies.

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Data availability All data are available on request.

Code availability Not applicable.

Declarations

Conflict of interest Casagrande, Quintavalle, Fabris and Lucangelo are co-inventors of the European patent EP 3 308 819 A1, entitled “Apparatus To Identify Respiratory Asynchronies In An Assisted Breathing Machine” [25].

Ethical approval Ethical approval was waived by the local Ethics Committee of Corporaciò Sanitaria Parc Taulì, Sabadell, Spain, in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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