Exploratory Analysis of Ventilation Signals from Resuscitation Data of Newborns

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Abstract: Prevention of neonatal mortality and morbidity because of birth asphyxia is still a major challenge. In a non-breathing baby, resuscitation including manual ventilation should start within one minute after birth. Information extracted from ventilation signals might give a good indication of the effectiveness of therapy. A framework for exploratory data analysis was developed facilitating the development of signal parameters to identify the relationships between certain signal characteristics and various outcome groups. Low p-values found for some ventilation parameters indicates that the method presented could be useful in discovering factors and parameters that might be important for the outcome of ventilation therapy and for guiding further treatment.

1 INTRODUCTION

In an asphyxiated infant, positive pressure ventilation should commence within 1 minute after birth according to the International Liaison Committee on Resuscitation guidelines for neonatal resuscitation (ILCOR, 2010). Ventilation of newborns is challenging because it is time critical and involving complicated interactions between newborn pathophysiology and the clinical treatment. Determining beneficial characteristics of different ventilation parameters is necessary for clinicians in order to improve neonatal treatment and survival.

Five ventilation parameters were derived from bag mask ventilation pressure and flow signals. The hypothesis is that certain characteristics of these ventilation parameters could relate to specific neonatal conditions and improvement in outcome and thus be useful for guiding further treatment. “Apgar score” is an universal scoring system to evaluate the clinical status of the baby after birth, usually performed at 1, 5, 10 and 20 minutes. The evaluation is based on five subjective factors: Appearance (skin color), Pulse (heart rate), Grimace response (or reflex irritability), Activity and muscle tone, and Respiration (breathing rate and effort). Each factor is scored on a scale from 0 to 2 (the best score). Thus, the total score is from 0 to 10. The 1-minute score reflects the immediate condition of the baby after birth, whereas the 5-minute score shows how the cardio-respiratory transition from intrauterine to extrauterine life progresses. In this exploratory study, the change in Apgar score from 1 minute to 5 minutes is used as the measure of effectiveness of ventilation. An improved score for an asphyxiated baby, implies a positive response to the ventilation given and vice versa.

The International Liaison Committee on Resuscitation and the World Health Organization provide healthcare workers with guidelines for neonatal resuscitation (ILCOR, 2010; WHO, 2011). However, the optimal values of pressure, volume and frequency during positive pressure ventilation of newborns are still unclear although research is growing in this field (Perlman et al., 2012). The interaction between mechanical ventilation parameters and the physiology of the lungs has been investigated, concluding that it was difficult to select an effective respirator setting because the results were highly dependent on the char-

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acteristics of the newborns population (Ramsden and Reynolds, 1987). Software systems to extract ventilation parameters and to provide decision support during mechanical ventilation has been previously studied (Ciurea et al., 2011; Tehrani, 2011; Schulze et al., 1984). However, very little research is done to understand the different initial situation of manual positive pressure ventilation during resuscitation at birth. In this previous group work (Vu et al.,), we have analysed ECG signal from the novel Laerdal Newborn Resuscitation Monitor (LNRM) developed by Laerdal Global Health to investigate effects of ventilation parameters during initial resuscitation on heart rate changes.

In this work, by using signal analysis of waveforms in the recorded biophysical signals, we detect and parameterize events defined as inflations from the start of pressing the bag to the end of exhalation. Furthermore we propose a data explorative approach to identify ventilation parameters which might be determinant for beneficial neonatal outcome.

2 MATERIALS AND METHODS

2.1 Dataset

This exploratory analysis is based on data from the "Safer Births" project at Haydom Lutheran Hospital in Northern Tanzania. Haydom is a resource limited rural hospital with a great shortage in health care staff. During the study period, basic newborn resuscitations (i.e. stimulation, suction, and bag mask ventilation) and Apgar scoring were predominantly conducted by midwives, always observed by trained research assistants recording the findings on a data collection form. The implementation of the research project was approved by National Institute for Medical Research (NIMR) in Tanzania and Regional Committee for Medical and Health Research Ethics (REK) in Norway.

The Laerdal Newborn Resuscitation Monitor (LNRM) is a resuscitation monitor designed for research use in low resource settings where newborn resuscitations usually are performed by a single care provider. The whole set up is presented in figure 1.

LRNMs were employed in the labour ward of Haydom to measure various physiological data such as ECG signals through dry-electrode ECG measured on the thorax, CO_2 concentration, airway pressure and flow signals. ECG signal was sampled at 500 Hz, CO_2 signal was sampled at 20 Hz, pressure and flow signals were sampled at 100 Hz. A flow-sensor (Acutronic Medical Systems AG) is arranged between the face mask and the resuscitator bag. The airway adapter also connects two plastic tubes with the LNRM: one tube draws a small sample of exhaled air (50 ml/min) for standard CO_2 measurement (Masimo Sweden AB), and one tube is used for standard pressure measurement.

The dataset contains recording of 218 infants collected between July 2013 to June 2014 with complete signals. Quality control and management of all research data were performed on a daily basis by local research staff.

2.2 Processing and Parameterization of Ventilation Signals

To characterize the ventilations given by healthcare workers, we detected bag-mask ventilation events by using two signals: the airway pressure and the flow signals from the ventilation sensors. We define five ventilation parameters: average ventilation frequency, average peak inspiratory pressure (PIP), average expired volume, initial peak inspiratory pressure, and ventilation time percentage (the percentage of time of ventilation sequences in the total time of ventilation including pauses).

Airway Pressure Signal

In this paper, the term "ventilation event" corresponds to pressing the ventilation bag. The start of one ventilation event is detected when the value of pressure increases from baseline then exceeds a threshold of 5 mbar. The PIP of each ventilation event is the maximum value of the pressure signal as illustrated in figure 2.

A "pause" is defined as the period of time when the pressure signal value is lower than 5 mbar for more than 3 seconds. A "ventilation sequence" represents several continuous ventilation events without pauses. This is explained in the figures 3 and 4. The "total ventilation time" is the time from the first to the last ventilation event including pauses as shown in figure 5. Among the five ventilation parameters, four of them are derived from the pressure signal and can be described as follows:

- The average ventilation frequency ($f_{v_{av}}$) is the ratio of total number of ventilation events (n_{v_i}) over the sum of duration of each ventilation sequence (t_i). This parameter represents how fast healthcare workers press the ventilation bag.

$$f_{v_{av}} = \frac{\sum_i n_{v_i}}{\sum_i t_i} \tag{1}$$

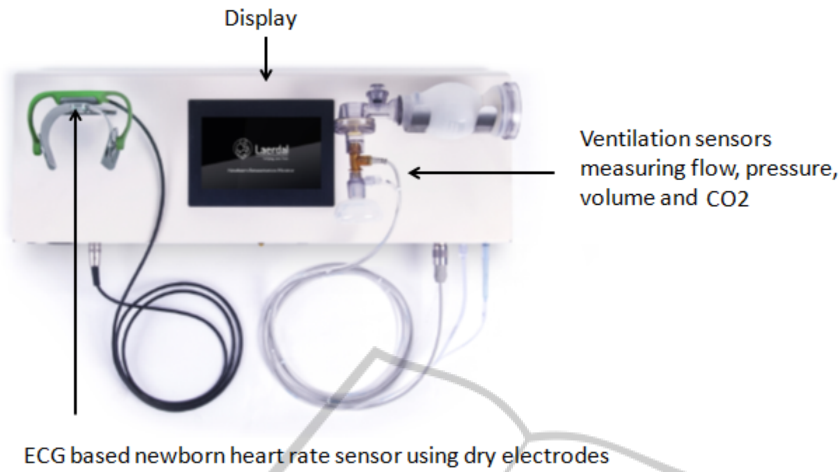


Figure 1: Laerdal Newborn Resuscitation Monitor.

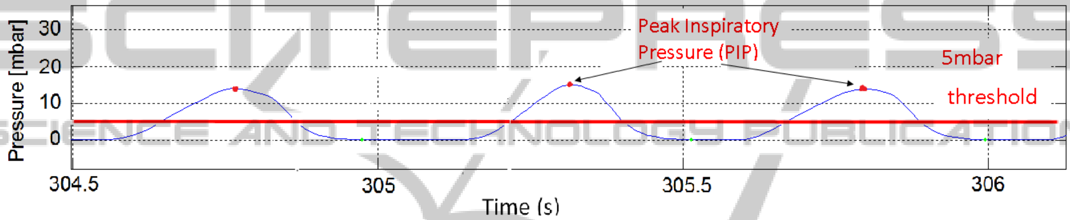


Figure 2: Pressure signal - Detection of ventilation event and PIP.

- The average PIP (PIP_{av}) is the "weighted average" of mean values of PIPs of ventilation sequences ($\overline{PIP}$) where the weight is the duration of each ventilation sequence (t_i), which means that the long sequences dominate to the PIP_{av} more than the short sequences. This parameter shows the average peak inspiratory pressure applied for ventilation.

$$PIP_{av} = \frac{\sum_i \overline{PIP}_i * t_i}{\sum_i t_i} \tag{2}$$

- Initial peak inspiratory pressure (PIP_{init}) is the first average PIP value of the first ventilation sequence that has the duration longer than 0.5 second. This parameter represents the initial peak inspiratory pressure to open the lung.
- Ventilation time percentage (VT_{PRC}) is the percentage of sum of duration of all ventilation sequences in the total ventilation time (T_v). This parameter shows the percentage of time the rescuer spending on ventilation during the whole ventilation procedure. For example, VT_{PRC} = 60 % means that 60 % of the total ventilation time is spent for ventilation effort and 40 % of time could be used for other resuscitation methods.

$$VT_{PRC} = \frac{\sum_i t_i}{T_v} * 100\% \tag{3}$$

Volume Waveform

The volume waveform is integrated from the flow signal which is measured by the hot-wire flow sensor (Acutronic Medical Systems AG). The expired volume is the amount of air going back through the flow sensor after one inflation. The expired volume is the volume drop from the maximum value to zero or to a non zero value when there is mask leakage. The average expired volume (ExV_{av}) is the mean of all expired volume values. Figure 6 shows one inflation cycle.

2.3 Statistical Approach

We want to investigate if certain patterns of these parameters show association with specific neonatal outcomes (e.g.,improved Apgar score from 1 to 5 minutes) when comparing different groups of babies. P-value method for statistical significance test among groups of babies were calculated by using Wilcoxon rank-sum testing in Matlab which is a non-parametric method for non-normal distributed data. P-values from the significance tests are used to represent the discriminative capability of different ventilation parameters. The criteria for grouping patients is based on delta Apgar score (ΔAP) which is the change from Apgar score at 1 minute (AP1) to Apgar score at 5

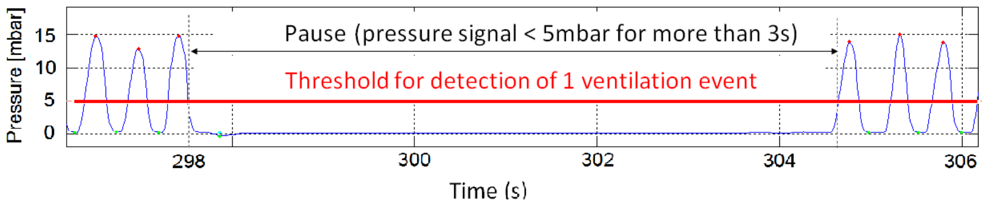


Figure 3: Pressure signal - Two consecutive ventilation sequences.

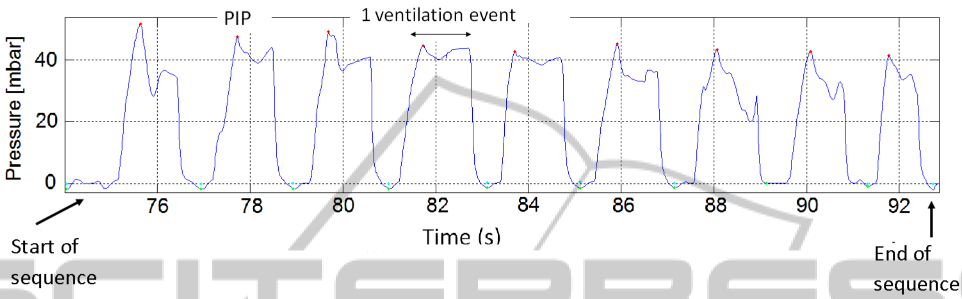


Figure 4: Pressure signal - One continuous ventilation sequence.

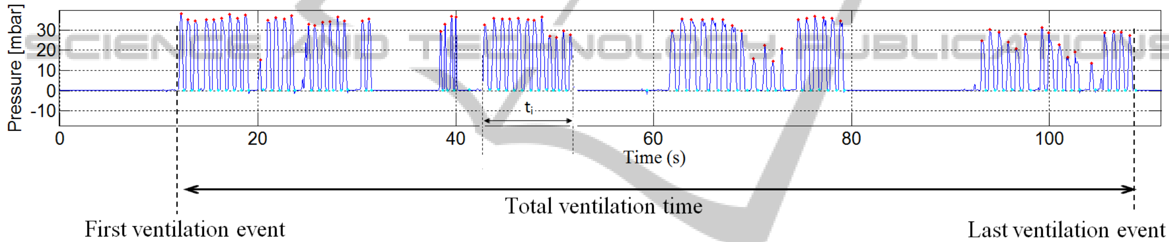


Figure 5: Total ventilation time is the duration from the first ventilation event to the last one.

minutes (AP5) defined in equation 4.

$$\Delta AP = AP5 - AP1 \tag{4}$$

Group 1 has $\Delta AP <=$ threshold and group 2 has ΔAP $>$ threshold. Therefore, group 2 is considered to be the improved group (or the group with positive outcome). For example, if the Apgar score at 1 minute and Apgar score at 5 minute of a baby are 3 and 7 respectively, then the ΔAP is 4. And if the threshold is 2, then the baby is categorized into group 2. A low p-value implies the difference in medians of the two groups and that the corresponding ventilation parameter could have important effect on the result of the treatment (i.e. improvement in Apgar scoring from 1 minute to 5 minutes).

2.4 Proposed Framework for Data Exploration

Evaluation Criteria for the Effectiveness of Ventilation during Resuscitation

We use ΔAP (equation 4) as a criteria to evaluate the effectiveness of the ventilation effort. For a low p-value, ΔAP above a threshold might indicate an appropriate resuscitation whereas ΔAP equal or below a threshold could imply an ineffective one.

Grid of P-values

To see how the medians of ventilation parameters affect various subsets of patients with different starting conditions, the data were segmented based on Apgar score at 1 minute. A grid of p-values is defined as a plot where x (Apgar score at 1 minute lower boundary) and y (Apgar score at 1 minute upper boundary) axes define the range of the Apgar score at 1 minute and colors represent different p-values. Each point on the grid corresponds to a subset of patients having the Apgar score at 1 minute in the range indicated by the two axes of the grid (Apgar score at 1 min lower boundary, Apgar score at 1 min upper boundary). For example, the coordinate (x = 3, y = 8) includes a subset of babies having Apgar score 1 minute in the range from 1 (lower boundary) to 8 (upper boundary). This subset of patients is categorized into two groups according to their ΔAP values. We compute the p-value of each subset to test the difference in medians of the

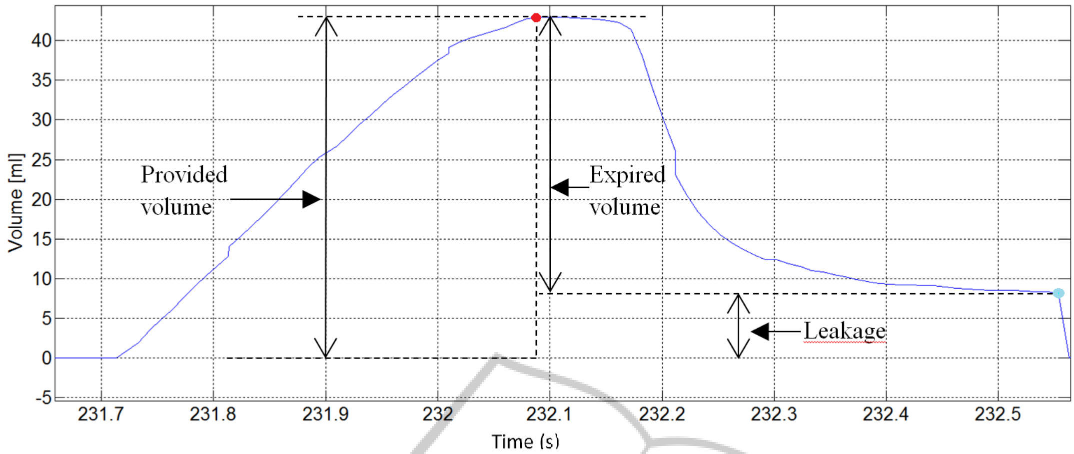


Figure 6: Volume waveform of one inflation cycle.

two groups defined by a threshold value of ΔAP. The p-value is assigned a color value by using a color map. The low p-values (< 0.05) are illustrated as triangles otherwise as circles. Group 2 is the improved group with higher ΔAP, thus we illustrate the relative difference between the median value of group 2 (the group with the positive outcome) compared to group 1 (the group with the negative outcome) by using upward and downward triangles. The upward triangles represent the higher median value of group 2 compared to group 1 and vice versa. For example, if the p-value is low (< 0.05) and group 2 has a higher median value than group 1, the corresponding point in the grid is represented by an upward triangle, otherwise a downward triangle. The size of each point on the grid is proportional to the number of patients in the smallest group, thus illustrating the size of data used for statistical testing. For example, group 1 has 34 patients and group 2 has 45 patients, then the size of the circle or the triangle is proportional to the size of group 1 that has the smaller number of patients.

3 EXPERIMENT AND RESULTS

To find an appropriate threshold value of ΔAP for our experiment, a histogram representing number of patients with different Apgar score at 1 minute and Apgar score at 5 minutes is shown in figure 7.

The blue diagonal line on the histogram represents the ΔAP equal to 0 since the Apgar score at 5 minutes is equal to Apgar score at 1 minute. The line also separates the histogram into two parts: the left one with $\Delta AP > 0$ (Apgar score at 5 minutes $>$ Apgar score at 1 minute) and the right one with $\Delta AP < 0$ (Apgar score at 5 minutes $<$ Apgar score at 1 minute). The lines parallel with the main diagonal represent different ΔAP thresholds and this is a visualization of how threshold values separate our data into groups with positive outcome and negative outcome. We experimented with $\Delta AP = 2$ and $\Delta AP = 3$ to ensure that the number of babies in each group was sufficiently large. Each ventilation parameter has two p-value grids corresponding to these different threshold values of ΔAP. Figure 8a is the p-value grid of PIP_{av} using $\Delta AP = 2$ and figure 8b is the corresponding box plots of the red-circled point in the grid (the color bar next to the p-value grid represents ranges of p-values). The number on each box plot represents the number of babies in each group. The box plots show the difference in medians of two outcome groups, specifically, group 2 has the lower median value of PIP_{av}.

Figures 9 and 10 show p-value grids for other ventilation parameters with $\Delta AP = 2$ and $\Delta AP = 3$ respectively.

4 DISCUSSION

P-values below significance level (0.05) were found for some ventilation parameters: average peak inspiratory pressure (PIP_{av}), average expired volume (ExV_{av}), and ventilation time percentage (VT_{PRC}) when comparing different thresholds of ΔAP scores. In the p-value grids, points in the top left corner usually have no low p-values. There could be two reasons: one is that for these points we include a wide range of patients or the diversity of the samples are high therefore there is no big difference in medians. The other reason may be that babies born with a high Apgar score will improve independently of performance of ventilation. For points in the left bottom of the grid that correspond to severely asphyxiated babies at birth, there are no low p-values either. Effec-

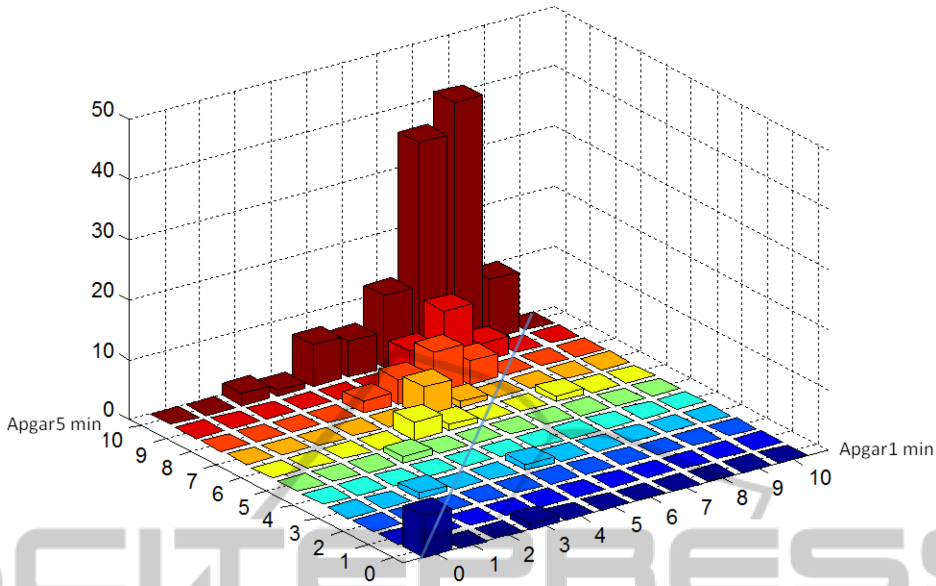
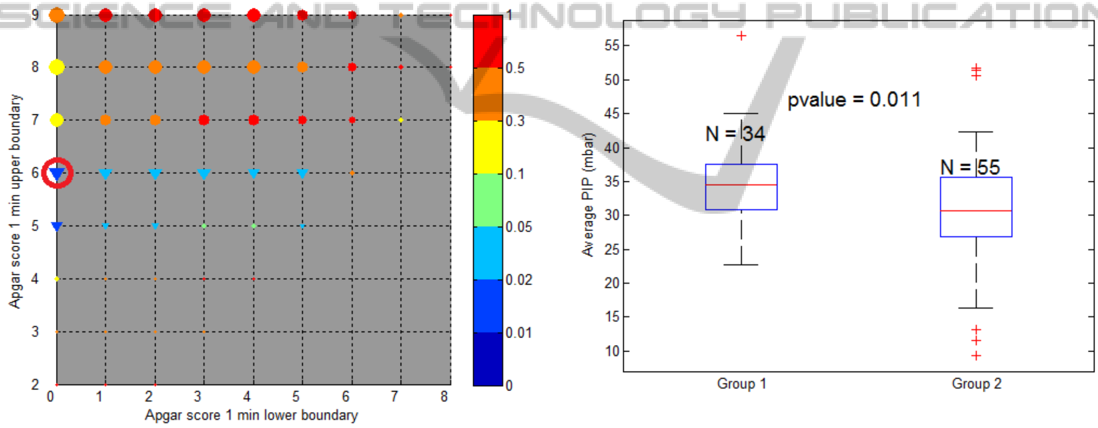


Figure 7: Histogram of distribution of data for Apgar score at 1 minute and 5 minutes.



(a) (b)

Figure 8: (a) P-value grid for average PIP (PIP_{av}), ΔAP threshold = 2. The low p-values (< 0.05) are illustrated as triangles otherwise as circles. The upward-pointing triangles indicate the higher medians and the downward-pointing triangles indicate the lower medians of group 2 (the improved group with higher ΔAP) in comparison with group 1. The size of each point in the grid is proportional to the minimum number of patients between two groups. (b) Box plot for the red-circled point corresponding to a subset of patients having Apgar score 1 minute in the range indicated by the coordinate of that point in the grid (Apgar score 1 minute ranging from 0 to 6). P-value obtained from statistical significance test on PIP_{av} for this subset is 0.011. The median value of group 2 (including infants in that subset having $\Delta AP > 2$) is 30.68, which is lower than the median value 34.51 of group 1 (infants with $\Delta AP <= 2$), thus the downward-pointing triangle is used.

tive bag mask ventilation (opening of functional residual capacity) maybe more difficult in these babies and ventilations alone might not be sufficient to improve outcome. In this low-resourced setting, cardiac compression, intubation, and intravenous medication are not performed. In our exploratory data, we find low p-values indicating different medians of ventilation parameters more often in the middle range (not very low and not very high) of Apgar score at 1 minute.

This exploratory test suggests that infants with a low Apgar at 1 minute who improved to a higher Apgar score at 5 minutes have a lower median value of ventilation time percentage (VT_{PRC}). This could possibly be explained by that the importance of stimulations was not included in the analysis. Therefore, this interpretation needs to be further explored by integrating information about stimulation effort into VT_{PRC} parameter in future work.

The explorative nature of this analysis imposes a limitation that should be noted. As the number of

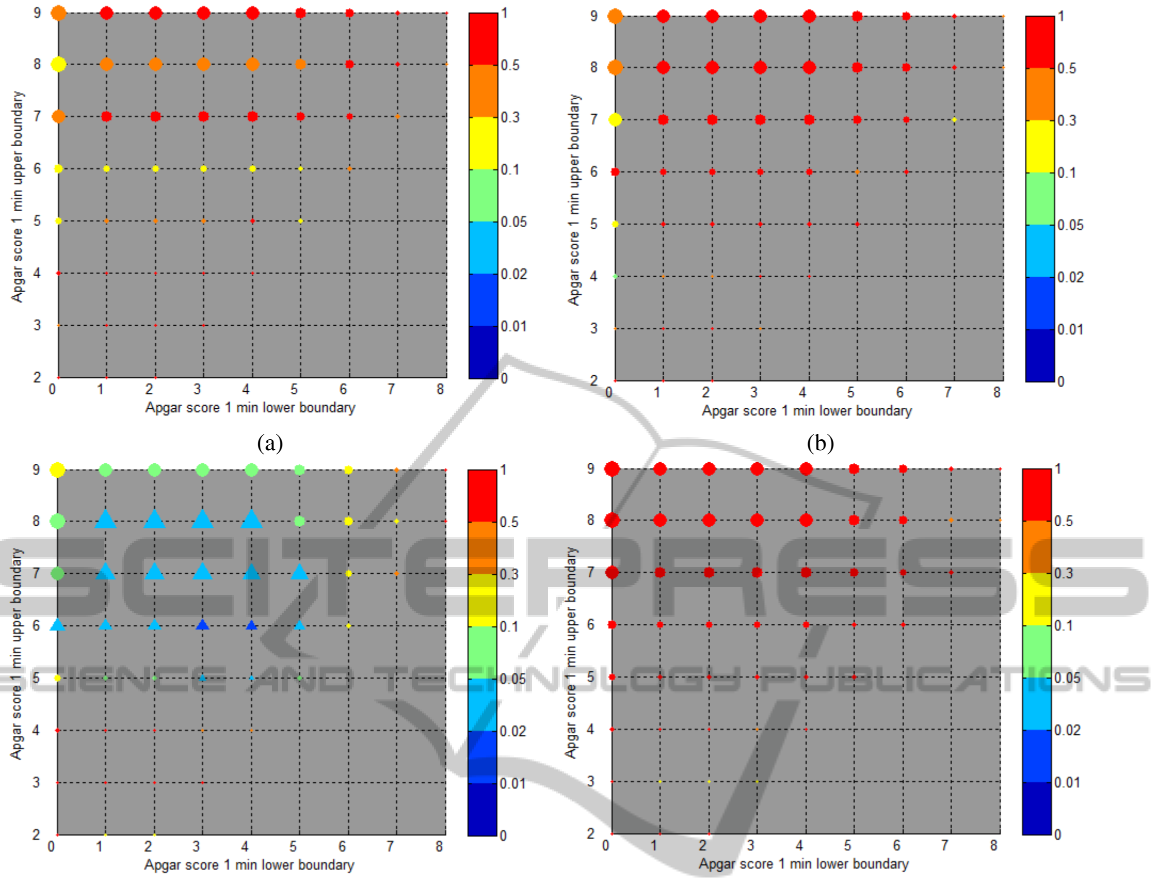


Figure 9: $\Delta AP = 2$. (a) P-value grids for initial PIP (PIP_{init}). (b) P-value grids for ventilation frequency ($f_{v_{av}}$). (c) P-value grids for average expired volume (ExV_{av}). (d) P-value grids for ventilation time percentage (VT_{PRC}).

groups tested are exhaustive, it is expected that some of the low p-values might have appeared by chance. The intent of the analysis is to identify ventilation parameters to investigate further in future studies.

5 CONCLUSIONS AND FUTURE WORK

In this paper, we illustrate a way to process ventilation signals from bag-mask ventilations recorded in a Newborn Resuscitation Monitor, define ventilation parameters and propose a framework for data exploration. We reveal the possibility of using information extracted from ventilation signals related to improved Apgar scoring to potentially describe beneficial value-ranges of different ventilation parameters.

Some ventilation parameters such as average peak inspiratory pressure (PIP_{av}), average expired volume (ExV_{av}), and ventilation time percentage (VT_{PRC}) were identified by the analysis. These findings might indicate that these parameters could be determinant factors for beneficial positive pressure ventilation. As this is a study using exploratory data analysis, the findings needs to be further investigated by using new data.

For future work, this framework of data analysis could be extended to test the discriminative capability of different ventilation parameters with other outcome definitions as well. We might also count the stimulation time as the ventilation time when we derive the ventilation time percentage (VT_{PRC}) parameter. There is also a possibility to combine some ventilation parameters to investigate their effect altogether on the resuscitation outcome.

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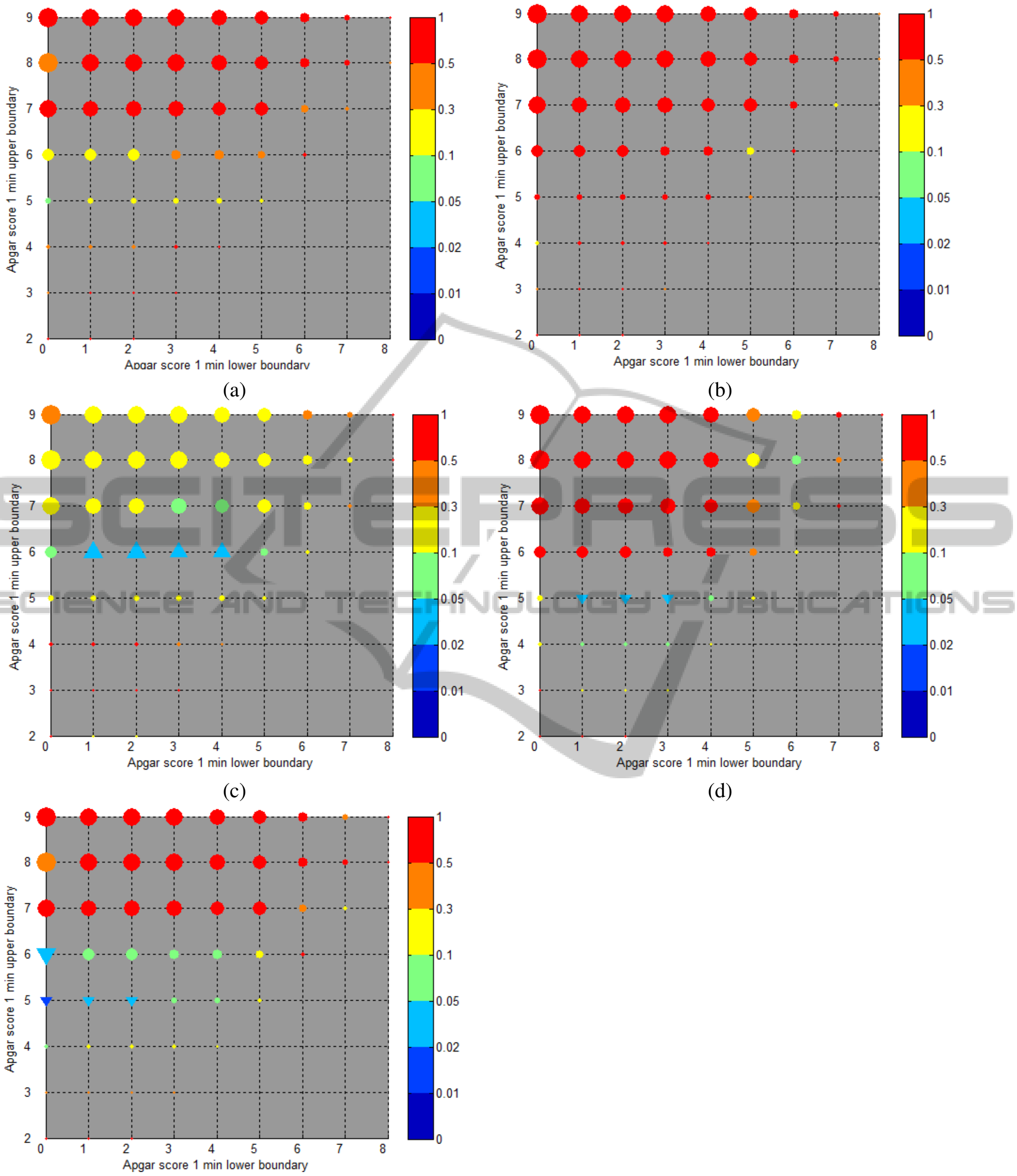

(a) (b) (c) (d) (e)

Figure 10: $\Delta AP = 3$. (a) P-value grids for initial PIP (PIP_{init}). (b) P-value grids for ventilation frequency ($f_{v_{av}}$). (c) P-value grids for average expired volume (ExV_{av}). (d) P-value grids for ventilation time percentage (VT_{PRC}). (e) P-value grids for average PIP (PIP_{av}).

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