Proceedings of the World Congress on Engineering 2007 Vol II
WCE 2007, July 2 - 4, 2007, London, U.K.

Pulse Transit Time and Inspiratory Resistive Load as a Marker for Inspiratory Perception in Children

Jong Yong Abdiel Foo, *Member, IAENG*, Stephen James Wilson, and Chu Sing Lim

***Abstract*— Inspiratory resistive load (IRL) has been used as part of clinical tools to evaluate respiratory responses of a child like depth of inspiratory efforts and perception of the inspiratory load. These responses have shown to be important to monitor the prognosis of asthma and sleep apnea. Minimally invasive instrumentations are generally preferred for children if extended monitoring is required. A parameter termed pulse transit time (PTT) has been suggested to be a surrogate marker of inspiratory efforts in respiratory sleep studies. In this study, 10 healthy children (8 male; aged 8.3 ± 2.6yr) were recruited to breath through a customized facemask with four different inspiratory load settings in their wakeful state. PTT technique was used to determine its potential in assessing a child's perception of an inspiratory load. The results show that relative air pressure variations within the facemask can relate to changes observed in PTT in a significant manner (p<0.05; R^2=0.627). The breathing frequency during each test activities also indicated that there was a general lower trend when a higher valued IRL is introduced. Essentially, a relative lower mean PTT value was observed with a higher inspiratory load (p<0.05; R^2=0.643). The findings herein can suggest that this simple measure can be a suitable candidature for inspiratory effort monitor in the pediatrics population especially when prolonged monitoring is required.**

***Index Terms*— Control of breathing; breathing pattern; loaded breathing; non-invasive monitoring; pediatrics.**

I. Introduction

In physically exhaustive activities like exercising or resistive breathing, development of respiratory muscle fatigue may be responsible for the changes in breathing pattern, respiratory mechanics or the respiratory muscle recruitment observed in the course of these activities [1]. The effects of rapid shallow breathing (or increased breathing frequency (BF) and decreased tidal volume) during these activities have been well-described [2]. Other studies have suggested children with certain medical conditions can have unique breathing patterns in response to provocative testing. Particularly, the inspiratory resistive load (IRL) is used to study asthmatic children [3], those with neuromuscular disease [4] or sleep apnea syndrome [5]. Minimally invasive instrumentations are generally more accommodating in order to evaluate responses to the introduced IRL like depth of inspiratory efforts and perception of the inspiratory load, especially for children.

A simple and non-invasive physiologic parameter known as pulse transit time (PTT) has shown its potential in respiratory sleep studies. The correlation of esophageal pressure variations induced by episodes of augmented airways resistance and PTT fluctuations during respiration has been demonstrated to be significant [6]–[7]. PTT is the time taken for the arterial pulse pressure wave to travel from the left ventricular to a peripheral site, commonly a finger or toe. This technique is usually measured as the time delay between the R-wave of the electrocardiogram (ECG) and its subsequent arrival at the selected periphery using the photoplethysmography (PPG) method [7]–[8]. The principal determinant by which these waves propagate is the degree in stiffness of the arterial wall and this is highly dependent on the instantaneous blood pressure (BP). As the BP increases, this affects the geometric and mechanical properties of the arterial wall thus, leading to an increase in its stiffness. During such occurrences, these pulse waves propagate faster and thereby decreasing the PTT duration [6], [8]. In this study, the breathing patterns of healthy children were studied when four different inspiratory settings were used in their wakeful state.

Hence, the following objectives were set for the present study: (1) formulate the relation between the changes in inspiratory efforts with PTT and (2) evaluate the trend of IRL to mean PTT values obtained from these children.

II. Materials and Methods

A. Subjects

This is a continuous investigation of a study conducted previously and documented elsewhere [9]. 10 healthy children (8 male and 2 female) were recruited as the study population.

Manuscript received January 16, 2007. This work was supported in part by the Biomedical and Pharmaceutical Engineering Cluster in the Nanyang Technological University, Singapore.

J. Y. A. Foo is with the Biomedical Engineering Research Centre, Nanyang Technological University, 50 Nanyang Drive, Research Techno Plaza, 6th Storey, XFrontiers Block, Singapore 637553 (phone: +65 6316 2957; fax: +65 6971 2274; e-mail: jong@ntu.edu.sg).

S. J. Wilson is with the School of Information Technology and Electrical Engineering, University of Queensland, St Lucia Campus, Brisbane, Queensland, Australia 4067.

C. S. Lim is with the School of Chemical and Biomedical Engineering, Nanyang Technological University, 16 Nanyang Drive, Singapore 637722.

Only those with no ischaemic feet or amputated legs observed, had a normal ankle-brachial pressure index ≥ 1.1, and were not obese with a body mass index ≤ 25.0 were included. To be eligible, they were not on medication or have any strenuous exercise 24hr prior to the study. Their mean age with their standard deviation (SD) was 8.3 ± 2.6yr (range 4 to 12yr). The parent(s) and they were given the study procedure and purposes verbally. Both informed consent and institutional ethical approval were obtained for the present study.

B. Experimental Materials

In order to simulate increased breathing efforts, a standard handheld pediatric flexible silicon oronasal facemask (AstraZeneca International, London, UK) was used. The choice to use this facemask was to allow the ease to remove it when necessary. The valve port was fitted with a customized adaptor with two openings and this was to ensure unidirectional airflow for the purpose of this study. On the inspiratory arm, this was where an IRL can be inserted. While the other opening acted as the expiratory end, a unidirectional valve was fitted to ensure that inspiration did not flow through this opening. No added resistance was applied to the expiratory port and a mechanical guard was fitted to prevent the child from holding onto the valve during the study.

An outlet was mounted on the customized adaptor to measure relative air pressure changes (ΔAir) in the facemask during the breathing cycle. A differential air pressure transducer (Micro Switch 140PC series, Honeywell Inc, New Jersey, USA) was used and calibrated with a manometer (Airflow Development Ltd, Buckinghamshire, UK). This measure was fed into a 16-channel PowerLab/16SP and recorded in its proprietary software, Chart version 5.2 (ADInstruments Corp, Colorado, USA). The recorded signals were sampled and stored at a rate of 400 samples per second. No signal conditioning was applied to these signals in the proprietary software. The inner diameter of the three chosen IRL was 3, 4 and 5mm that can simulate airway resistance of 46.9, 26.4 and 7.8cm $H_2O/l/s$ respectively. This resistance was linear over the airflow ranging from 0.10 to 0.25*l*/s and was selected as it was within the range for children used by others [5], [10]. Figure 1 shows the main apparatus used in this study including those that were used to simulate the increased breathing efforts activity.

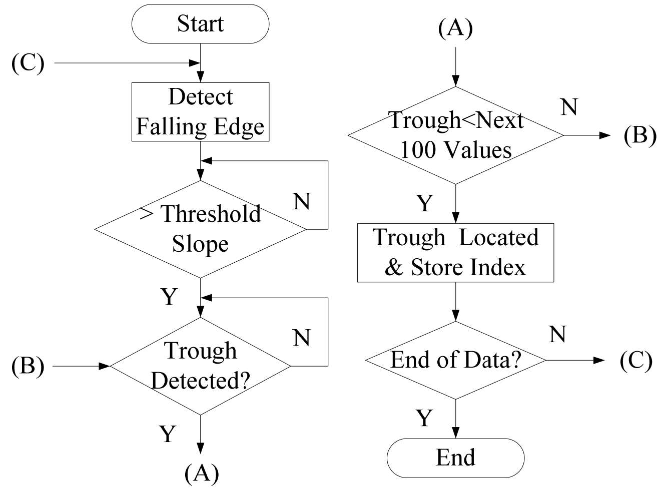

Figure 1: This flowchart shows transit time related calculations derived from the ECG and PPG signals used in the present study.

In order to calculate the corresponding PTT value, the ECG and PPG signals were attained from a single-lead monitor (S&W Medico, Teknik, Denmark) and a pulse oximeter (Novametrix Medical Systems Inc, Wallingford, USA) respectively. These signals were fed into the PowerLab system and recorded. In this study, the PTT calculation was implemented using the Matlab Release 14 (the MathWorks Inc, Natick, USA) software. A test program that predicted each corresponding ECG peaks was written using a slope detection algorithm to identify their rising edge. A differentiator then detected the peak of the ECG signal. Thereafter, a window of 100-recorded data following this detected peak was used to determine its validation. This was to minimize the false locating of peaks induced by ripples riding on the ECG signals. In the same manner, the peak of PPG signals was located and computed. The described algorithm of the PTT computation is as given in Figure 2.

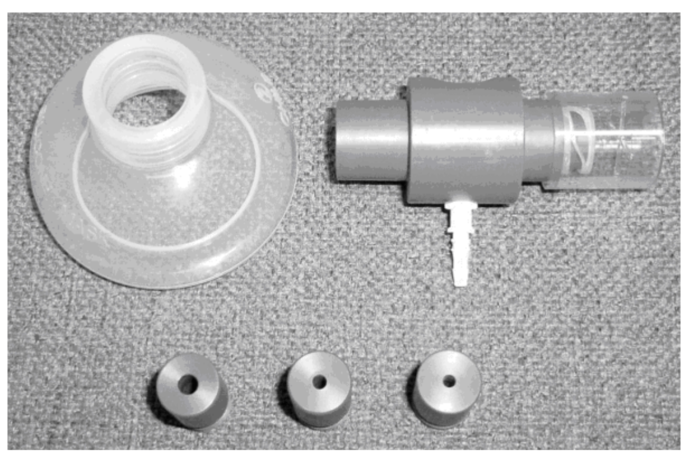

Figure 2: Customized apparatus used in this study to simulate increased breathing efforts; facemask, IRL and an adaptor including a unidirectional airflow valve, an air pressure measure outlet and mechanical guard

C. Experimental Protocols

All measurements of this study were conducted with the children in their supine posture while awake. Each child was asked to perform four test activities. The first activity was with the customized adaptor on facemask but having no inspiratory load mounted (regarded as the baseline value). Before any tested activity, the child was habituated to the surrounding and apparatus for 5min for cardiovascular stability. Thereafter, the first IRL was inserted onto the customized adaptor and recorded for 1min. The 1-minute duration was chosen because it was comparable to an apneic event and this was useful to study the child's perception of the induced inspiratory load [10]. This period also marked the physical limitation of most recruited children as there were notable motional artifacts on the recorded PPG signals that can complicate the results. The second and third IRL were sequentially introduced in the same manner with a 5-minute rest interval between each activity. The order of the IRL used in the study was a random selection for each child.

D. Data Analysis

In order to minimize inter-subject variability, mean value of the measured parameters obtained in baseline was used as the reference for the three IRL activities for that subject only. From the ΔAir parameter, the corresponding BF and breathing effort during each of the test activities were derived. Similarly, mean PTT and relative changes in PTT (ΔPTT) from its baseline value during each activity were recorded. Statistical analysis was performed using the Excel 2003 (Microsoft Corporation, Seattle, USA) and Matlab Release 14 packages. Paired Student's *t*-test was used to test for significant differences for data obtained during the three IRL test activities against their baseline value. In this study, a value of $p<0.05$ was considered as statistically significant.

III. RESULTS

Data were successfully recorded from the children during all four breathing test activities. These measurements were computed as ventilation responses to the introduction of the three different IRL against their corresponding baseline. The results of ΔAir parameter during tidal breathing were not included as most of its readings could not be readily registered. There was significant ($p<0.05$) incremental trend for both ΔAir and ΔPTT values with the increasing inspiratory load. This was expected as a higher mechanical inspiratory was required by the child to ventilate the airways. Figure 3 shows the correlation between the two parameters.

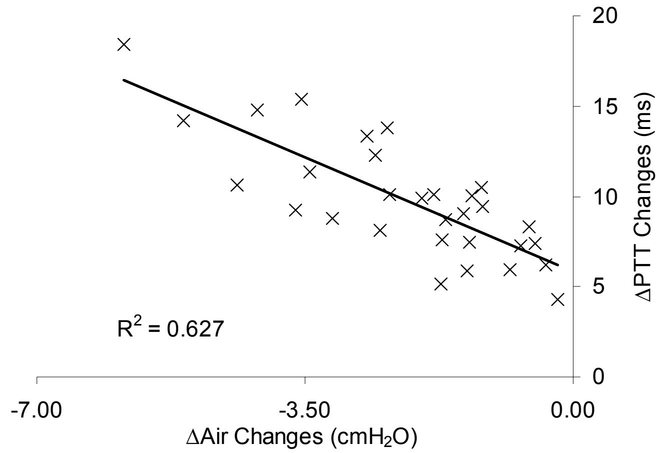

Figure 3: This plot illustrates that the ΔPTT trend is similar to that of ΔAir where it shows an incremental increase with a higher inspiratory load.

It was observed that most subjects exhibited a lower BF when a higher IRL was introduced except for subject #7 and #9 (but marginal difference only) as given in Table 1. With a general lower BF and increased breathing efforts, the corresponding effect on PTT measurements was a significantly ($p<0.05$) lower nominal mean value as presented in Figure 4. This can suggest that a lower mean PTT value can be perceived by the child as a greater valued inspiratory load.

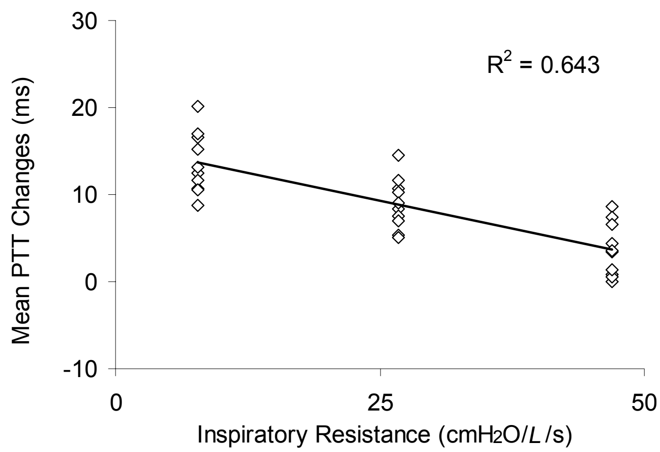

Figure 4: The results of mean PTT plotted against inspiratory resistance shows a reduction trend. This can suggest that with an increased inspiratory effort but lower breathing frequency, a higher valued IRL can be reflected by a lower mean PTT value.

Child	7.8cm $H_2O/l/s$ Load	26.7cm $H_2O/l/s$ Load	46.9cm $H_2O/l/s$ Load
1	16	13	11
2	20	14	10
3	25	21	16
4	23	19	16
5	18	15	13
6	22	17	14
#7	17	18	16
8	20	18	14
#9	19	17	20

10	23	20	16
Mean	20.3 ± 2.91	17.2 ± 2.57	14.6 ± 2.88

Table 1: The breathing frequency during each test activities is recorded in this table. It can be observed that there is a general lower trend (except for subject #7 and #9) when a higher valued IRL is introduced. This may be the responses caused by the more rapid physical tiredness of the child when a higher resistive load is introduced.

IV. Discussion

From the present study, the contributors to the observed PTT changes during the increased breathing efforts are examined with the use of IRL. The pressure exerted on the respiratory airways during this inspiratory provocative test can induce changes in BF, ΔAir, PTT and ΔPTT. The results obtained indicate that ΔAir changes can be reflected by monitoring ΔPTT changes. This association is indirectly similar to that observed in the ΔAir parameter with increasing IRL value [5]. Furthermore, it has been shown that with a greater inspiratory resistance, the subsequent level of inspiratory efforts also increased [11]. With an increasing inspiratory effort to ventilate the airway, a progressive increase in the inspiratory afterload to the left ventricle can occur and thus impairing its subsequent emptying during expiration [12]. This may also lead to an increase in right ventricular preload to produce substantial inspiratory increased in right ventricular end-diastolic pressure [13]. Essentially, the observation on mean PTT change trend can be indicative of the perception of the inspiratory load as demonstrated in the present study.

Previous research have validated the PTT technique to be a non-invasive approach in the monitoring of BP and/or heart rate (HR) changes in studies relating to cardio-vascular [14]–[15] and cardio-respiratory [6], [8]. However, the potential of using PTT signals to derive inspiratory perception has yet to be well-studied in children especially its usefulness in events of increased breathing efforts. From this study, it can be observed that PTT has the sensitivity to monitor this parameter not only in tidal breathing but also during induced inspiratory loads in children. With its signal components synchronous to both cardiac and respiratory rhythms, PTT signal can be a valuable mean to monitor not only for BP and HR changes, but also inspiratory perception as demonstrated in this study. This can be useful for children whom cannot tolerate or cooperate with more intrusive technique like nasal cannula, especially in prolonged monitoring such as during respiratory sleep studies [16]–[17]. In these studies, increased inspiratory effort is usually monitored as part of the polysomnographic protocol to identify occurrences of obstructive respiratory events. The potential of using PTT-derived marker of increased inspiratory efforts (or equivalent obstructive respiratory events) as indicated in this study is promising. However, further investigations are still required to verify its suitability and utility as a measure in these night-long studies.

The characteristics of the PPG pulse signal (which is one of the two essential waveforms in the calculation of PTT) are body site specific [18]. This means that pulses from the various peripheral sites showing differences in PTT value, strength as well as shape, and variation of each over time. Moreover, more recent studies on multi-site PPG measurement also indicated that the peripheral pressure at each peripheral sites influences the pulse arrival times and therefore relative pulse wave velocities. Particularly, any differences in vessel properties can affect the times and shapes of the rising edge and falling edge of the pulse. However in these studies, they have also suggested that any notable differences may indicate a significant pressure, resistance or compliance difference that is more likely to be associated with pathological changes [19]–[20]. Based on these understanding, adopting different peripheral sites for inspiratory perception measurements should not affect its accuracy in a significant manner though this does warrant further investigations to fully comprehend it.

It is acknowledged that there are some limitations to the present study. Firstly, there can be differences in vascular compliance in children and their corresponding transit time can vary. The present study only explores the relative changes observed in PTT to derive its findings. Moreover, PTT is recommended to be used as a semi-quantitative measure [14]. In addition, children with pathological conditions were not part of the study. Thus, it can be a further study where their inspiratory efforts and perceptions of inspiratory loads can be compared with those of the normal using the PTT technique.

V. Conclusions

Previous studies have shown that the PTT technique can be a suitable candidature in respiratory sleep studies. However, limited study has been conducted to understand its use to indicate the perception of inspiratory loads for children. From the present study, it can be seen that a higher inspiratory efforts may be reflected as a lower mean PTT. This measure may be a semi-quantitative measure but it is simple and more tolerable for children. This can be due to its non-invasive nature and especially useful when prolonged clinical monitoring is required.

Acknowledgment

The authors would like to acknowledge the support from the Biomedical and Pharmaceutical Engineering Cluster of the Nanyang Technological University towards this work.

References

[1] B. S. Krishnan, T. Zintel, C. McParland, and C. G. Gallagher, "Evolution of inspiratory and expiratory muscle pressures during endurance exercise". *J Appl Physiol*, vol. 88, pp. 234-245, 2000.

[2] P. Sliwinski, S. Yan, A. P. Gauthier, and P. T. Macklem, "Influence of global inspiratory muscle fatigue on breathing during exercise". *J Appl Physiol*, vol. 80, pp. 1270-1278, 1996.

[3] S. M. Julius, K. L. Davenport, and P. W. Davenport, "Perception of intrinsic and extrinsic respiratory loads in children with life-threatening asthma". *Pediatr Pulmonol*, vol. 34, pp. 425-433, 2002.

[4] D. Gozal, and P. Thiriet, "Respiratory muscle training in neuromuscular disease: long-term effects on strength and load perception". *Med Sci Sports Exerc*, vol. 31, pp. 1522-1527, 1999.

[5] C. L. Marcus, G. A. Moreira, O. Bamford, and J. Lutz, "Response to inspiratory resistive loading during sleep in normal children and children with obstructive apnea". *J Appl Physiol*, vol. 87, pp. 1448-1454, 1999

[6] J. Y. A. Foo, S. J. Wilson, A. P. Bradley, G. R. Williams, M-A. Harris, and D. M. Cooper, "Use of pulse transit time to distinguish respiratory events from tidal breathing in sleeping children". *Chest*, vol. 128, pp. 3013-3019, 2005.

[7] J. Y. A. Foo, "Pulse transit time in paediatric respiratory sleep studies". *Med Eng Phys*, vol. 29, pp. 17-25, 2007.

[8] E. S. Katz, J. Lutz, C. Black, and C. L. Marcus, "Pulse transit time as a measure of arousal and respiratory effort in children with sleep-disordered breathing". *Pediatr Res*, vol. 53, pp. 580-588, 2003.

[9] J. Y. A. Foo, and S. J. Wilson, "Estimation of breathing interval from the photoplethysmographic signals in children". *Physiol Meas*, vol. 26, pp. 1049-1058, 2005.

[10] Y. Tun, W. Hida, S. Okabe, Y. Kikuchi, H. Kurosawa, M. Tabata, and K. Shirato, "Inspiratory effort sensation to added resistive loading in patients with obstructive sleep apnea". *Chest*, vol. 118, pp. 1332-1338, 2000.

[11] T. D. Bradley, "Crossing the threshold: Implications for central sleep apnea". *Am J Respir Crit Care Med*, vol. 165, pp. 1203-1204, 2002.

[12] O. Marrone, and M. R. Bonsignore, "Pulmonary haemodynamics in obstructive sleep apnoea". *Sleep Med Rev*, vol. 6, pp. 175-193, 2002.

[13] L. Chen, and S. M. Scharf, "Comparative hemodynamic effects of periodic obstructive and simulated central apneas in sedated pigs". *J Appl Physiol*, vol. 83, pp. 485-494, 1997.

[14] R. P. Smith, J. Argod, J. L. Pepin, and P. A. Levy, "Pulse transit time: An appraisal of potential clinical applications". *Thorax*, vol. 54, pp. 452-458, 1999.

[15] S. Singham, L. Voss, J. Barnard, and J. Sleigh, "Nociceptive and anaesthetic-induced changes in pulse transit time during general anaesthesia". *Br J Anaesth*, vol. 91, pp. 662-666, 2003.

[16] A. Griffiths, J. Maul, A. Wilson, and S. Stick, "Improved detection of obstructive events in childhood sleep apnoea with the use of the nasal cannula and the differentiated sum signal". *J Sleep Res*, vol. 14, pp. 431-436, 2005.

[17] R. Budhiraja, J. L. Goodwin, S. Parthasarathy, and S. F. Quan, "Comparison of nasal pressure transducer and thermistor for detection of respiratory events during polysomnography in children". *Sleep*, vol. 28, pp. 1117-1121, 2005.

[18] E. Tur, M. Tur, H. I. Maibach, and R. H. Guy, "Basal perfusion of the cutaneous microcirculation: Measurements as a function of anatomic position". *J Invest Dermatol*, vol. 81, pp. 442-446, 1983.

[19] J. Allen, and A. Murray, "Age-related changes in the characteristics of the photoplethysmographic pulse shape at various body sites". *Physiol Meas*, vol. 24, pp. 297-307, 2003.

[20] J. Allen, and A. Murray, "Similarity in bilateral photoplethysmographic peripheral pulse wave characteristics at the ears, thumbs and toes". *Physiol Meas*, vol. 21, pp. 369-377, 2000.