This paper presents a pilot study investigating the usefulness of phonocardiography in assessing the hemodynamics of the patent ductus arteriosus (PDA) in preterm newborns. Nineteen infants have been examined, 11 with hemodynamically significant PDA, verified by echocardiography. Four of these newborns have been measured every day until the clinically verified closure of the PDA occurred. Murmur, related solely to PDA, was found in two infants but also some low frequency components of the heart sounds might indicate the state of the ductus arteriosus. Comparison of the heart sounds based on a cross-correlation method before and after the closure of the PDA is presented.

KEY WORDS
Biomedical signal processing, clinical assessment and patient diagnosis, phonocardiography, patent ductus arteriosus, preterm newborns

1 Introduction

The ductus arteriosus is an essential fetal vascular structure which connects the main pulmonary artery with the descending aorta. It shunts the blood coming from the right ventricle into the aorta due to the high resistance of the pulmonary circulation. Closure during pregnancy may lead to right heart failure. After birth, with the first intake of breath the lungs expand and the resistance of the pulmonary circulation decreases greatly allowing the development of the normal human circulation. Apparently the ductus arteriosus looses its purpose, moreover, the persistence of the ductal patency is abnormal. Under normal conditions functional complete closure occurs within the first day after birth [1] [2].

As known, the physiological impact and clinical significance of a PDA depends first of all on its size and the state of the underlying cardiovascular system. After birth, in case of PDA, a left-to-right shunt evolves due to the higher pressure in the aorta. This means an increased pulmonary fluid volume which may cause respiratory problems. Also the left atrium and ventricle have to compensate the increased fluid volume returning from the lungs and the "pressure leakage" in the aorta which may cause hypertrophy of the left atrium and ventricle.

Some symptoms for physical examination are murmur, located at the upper left sternal border, overactive precordium, tachycardia and bounding peripheral pulses due to the rapid decrease of the diastolic pressure through the ductus.

PDA can be "silent", which means that it doesn't produce clinical symptoms but it can be diagnosed by echocardiography.

The closure of the PDA may occur spontaneously or due to a surgical or transcatheter intervention. In case of preterm infants pharmacological closure is also possible [3][4].

In case of preterm neonates the risk of PDA is clearly much greater which is due to physiological factors related to prematurity [1]. The main diagnosis is done with echocardiography, which needs expertise and sophisticated equipment. Even though the assessment of hemodynamical significance is not obvious [5] [6], which means that the type and the timing of the treatment is also ambiguous. This project addresses exactly that point, namely whether phonocardiography is useful in diagnosing and monitoring PDA in preterm newborns, especially in the first days of life. A non-invasive and simple tool for assessing PDA would be of great importance.

This study is an extension of the research on fetal phonocardiography performed at the Péter Pázmány Catholic University, Faculty of Information Technology, Budapest [7].

2 Materials and Methods

In this section the measurement scenario and the analyzing methods are described.

2.1 Measurements

In this pilot study 19 preterm newborns have been examined, with an average of 2 measurements per infant, but with large deviations: only those newborns were examined several times which were diagnosed with PDA, those without PDA or with other cardiac malformation only once. Hemodynamically significant PDA was verified by echocardiography in case of 11 infants but only 4 of those
were examined over several days because the others had either also some other malformation or some other circumstances made further measurements not possible. In case of the 4 newborns mentioned above, the PDA was closed by means of pharmacological treatment.

These infants, except one, all weighed less than 2300 g at birth, with an average weight of 1600 g. Except one, all of them were less than 33 weeks of gestation, with an average of 30. They were examined on average on their 4th day after birth and those with PDA then every day until the complete closure of the PDA, which was verified by echocardiography (the maximum was 8 measurements on one infant). Three measurements had to be posteriorly excluded from the study because of the poor quality of the records since the measuring equipment was also developed during the study.

The measurements were made with a self-made electronic stethoscope (an electret microphone capsule, connected to a laptop, was joined together with a stethoscope head for infants). Each measurement consisted of about three 30 seconds long phonocardiographic records which were recorded at 44 kHz, with a resolution of 16 bits. According to our observation the main components of the heart sounds lie in the low frequency range, thus after preprocessing with a 2nd order Butterworth low-pass filter with a cut-off frequency of 400 Hz, the data was resampled at 1200 Hz and only the useful part of the record (at least 10 secs) was kept for further analysis.

2.2 Analyzing methods

The main goal was to investigate certain parameters of the heart sounds and, if present, of murmurs which could be related to some attributes of the duc tus arteriosus (e.g. width, velocity of blood flowing through it, etc.). It seemed obvious to investigate a characteristic heart sound for the given record. This was achieved by calculating a weighted average heart cycle assuming the following:

- an average heart sound can be calculated from similar heart cycles for at least the time of the measurement if no big change occurs in the cardiovascular system (often the same envelope was present over several days)
- murmurs caused by a given anomaly will appear in most of the heart cycles with similar envelope
- according to these measurements the usually occurring noise (e.g. from breathing machines) can be regarded as white noise in the investigated frequency range and thus averaging will suppress it

Due to the above mentioned aspects averaging seemed useful in enhancing the characteristics of the heart sounds and murmurs. The method is outlined in Fig. 1.

![Figure 1. General scheme of the analyzing method](image)

2.2.1 Heartbeat detection

The detection of the heart cycles and heartbeats was done with a heuristic method developed for fetal phonocardiography with a very good timing accuracy [8]. The outline of this heartbeat detection algorithm is as follows:

For a given phonocardiographic signal $s[k]$ lets define a kind of contrast enhancement by summing up the local differentials of the signal (1) on a short time window of length $a$ and taking the difference of neighbouring windows (2):

$$d[k] = s[k + 1] - s[k] \quad (1)$$

$$I_1[k] = \sum_{i=k}^{k+a} d[i] - \sum_{j=k-a}^{k} d[j] \quad (2)$$

Contrast enhancement is achieved by adding this local intensity difference $I_1[k]$ to the differential signal $d[k]$, and a secondary local intensity difference is calculated based on this resultant, like in (2) but with a greater time window of length $A$:

$$I_2[k] = \sum_{i=k}^{k+A} (d[i] + I_1[i]) - \sum_{j=k-A}^{k} (d[j] + I_1[j]) \quad (3)$$

Finally, the differences have to be computed in the same way as in (2) regarding the signal $I_2[k]$:

$$V[k] = \begin{cases} 
-\left(\sum_{i=k}^{k+A} I_2[i] - \sum_{j=k-A}^{k} I_2[j]\right) & \text{if } 0 \\
0 & \text{otherwise}
\end{cases} \quad (4)$$

Based on the values $a$ and $A$, the positive parts of the resultant signal $V[k]$ show the heart sounds or the cardiac cycles, as shown in Fig. 2.

As observable in Fig. 2, first heart sound (S1) and second heart sound (S2) detection can be achieved by finding the local maxima of $V[k]$. Classification of S1 and S2 sounds is based on the observation that S2 heart sounds have higher frequency components than S1 heart sounds, the systole (interval between S1 and S2) is usually shorter
than the diastole (interval between S2 and S1) and that these heart sounds alternate. Due to the short duration of the records it was possible to correct misclassified heart sounds. A completely autonomous detection and classification algorithm was not the goal of this study.

### 2.2.2 Cross-Correlation of the Heartbeats

Cross-correlation was used for the comparison of the different heartbeats. According to our measurements this was calculated with a 100 ms long time window for S1 heart sounds and with a 66 ms window for S2 heart sounds. For each heartbeat the normalized cross-correlation coefficient with all the other heartbeats was calculated. A threshold of 0.9 (in case of poorer quality data 0.8 or 0.85) was used for selecting the most typical heartbeat for the given record: that heartbeat was selected which had normalized correlation coefficients greater than the mentioned threshold with the greatest number of other heartbeats.

Temporal aligning was also performed with cross-correlation, namely by maximizing the cross-correlation between each heartbeat.

### 2.2.3 Averaging

The weighted average of heart sounds was calculated not only for the heartbeats but for the whole heart cycle, revealing potential murmurs, in the following manner:

$$\hat{b}_j[k] = \sum_{i=1}^{J} R_{ji} \cdot b_i[k - o_{ji}]$$  \hspace{1cm} (5)

where $\hat{b}_j$ is the average beat for the selected beat $b_j$, $J$ are the number of beats similar to beat $b_j$ with a normalized correlation coefficient greater than the given threshold, $R_{ji}$ is the maximal normalized correlation coefficient between beat $b_j$ and beat $b_i$, producing the offset of $o_{ji}$.

### 2.2.4 Analysis

The analysis of the characteristic heartbeats for a given record was done in the time and in the time-frequency domain due to the nonstationary nature of heart sounds. Short-time Fourier Transform was used to compute the time-frequency representation:

$$S_{bj}[k, f, h] = \sum_{l=-\infty}^{\infty} \hat{b}_j[l] \cdot h[l - k] \cdot e^{-j2\pi fl}$$  \hspace{1cm} (6)

where $h$ is the short-time analysis window. The optimal duration of the time window used to compute time-frequency representation of phonocardiograms is between 16 and 32 ms [9]. Here a 27 ms long Hamming window was used. Window shifting was 1 ms.

For the investigation in the time domain linear filtering was applied with different bandwidths. To avoid the phase distortion of IIR filters zero phase filtering was used: after filtering the data in the forward direction, the data was reversed and run back through the filter.

The analysis was mainly done by visual inspection of the envelope and the spectrogram looking for components which could be related to some attributes of PDA. This means that the length, the envelope and the frequency components of the heartbeats, and presence of split between the aortic and pulmonary heart sounds, and presence of murmurs and their frequency relationship were investigated.

### 3 Results and Discussion

Nevertheless preterms with PDA develop murmur usually only from the third day after birth [10], decision to treat PDA should be based also on clinical signs [6]. Thus a robust and sensitive heart sound and murmur inspection method would be of great importance since there is an extremely noisy auscultation environment in the clinical set-up.

The consecutive measurements of infants with PDA were investigated to find those properties of the heart sound which change with the closure of PDA. For this, the average beat of selected records from different measurements were compared.

The comparison of S1 sounds measured before and after the closure of the ductus arteriosus revealed that the temporal spreading of the energy of the first heart sounds decreased: in some cases faster attenuation is observable and usually the amplitude of the most dominant negative half wave increased (Fig. 3). This investigation also revealed that heart sounds remained similar for several days, thus comparison is possible.

Good results have been achieved by low-pass filtering the S1 heart sounds in case of more infants (Fig. 4), but further investigation is needed for this analysis.

The comparison of S2 sounds showed that in some cases the second heart sounds became split shortly after the closure of the PDA (Fig. 5). That means that there is an
increased time difference between the closure of the aortic and pulmonary valve. These two closure sounds make up the second heart sound.

Some solely PDA related, low grade, blowing murmurs were found in the records of two infants with echocardiographically verified PDA and no other cardiac disease. The time-frequency analysis of sections with murmur showed components with a dominant frequency of around 100 Hz. The main components of the heart sounds lie usually in the lower frequency range. Therefore high-pass filtering the records emphasizes the murmurs. As shown in Fig. 6, murmurs were found in the late systole. These murmurs always disappeared after the closure of the PDA.

By time aligning the systolic murmurs based on the maximization of the cross-correlation one can see that the murmur appears with similar components in many cardiac cycles, but its timing isn’t closely related to either S1 or S2 sounds (Fig. 7).

The results so far indicate that the assessment of PDA is not a trivial signal processing task. We hope that by extracting properties of heart sounds in a given record we can help the pediatricians in deciding the appropriate treatment. Further analysis and heart sound parameter extraction is needed (e.g. [11] [12]) for statistical verification of the investigation method.
4 Conclusion

The main goal of this pilot study was to investigate whether it is possible at all to develop a satisfactory phonocardiographic method for sensitive and specific assessment of PDA in preterm newborns in the first days after birth. From the measurements so far, several parameters were found which can be related to the state and closure of the PDA: the temporal energy spreading and some low-frequency components of the first heart sound, the splitting of the second heart sound and the presence and properties of murmurs could be linked with patent ductus arteriosus in preterm newborns. More measurements and further analysis are necessary.

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References


