Analysis of Breathing-related Variations in ECG-triggered Laser Doppler Perfusion Signals Measured on the Beating Heart during Surgery

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Abstract

Laser Doppler perfusion monitoring (LDPM) is a method to assess microvascular perfusion. A modified, ECG-triggered LDPM system has been developed to measure myocardial perfusion with minimum influence from heart motion. With this method, one systolic (PLS) and one diastolic (PLD) perfusion value is obtained.

The aim of this study was to analyse breathing-related variations in PLS and PLD measured during open-heart surgery. The phase delays between PLS, PLD, mean arterial blood pressure (MAP), heart rate and, indirectly, the respiration were determined.

MAP tended to be in phase with or precede the variations in PLD, i.e., PLD was at a maximum at the end of inspiration or at the beginning of expiration. No clear relation between PLS and any of the other signals could be found.

1. Introduction

A method to monitor myocardial perfusion during and after heart surgery has recently been developed [1,2]. The method is based on laser Doppler perfusion monitoring (LDPM), which is a technique that is widely used in microvascular research [3,4]. When LDPM is applied to a moving organ, large movement artifacts will be added to the signal. In the newly developed method the movement artifacts are minimized by ECG-triggering, i.e., the perfusion is measured in intervals in the cardiac cycle where the tissue motion is small. This technique has been evaluated during coronary artery bypass graft (CABG) surgery [5]. In that study, breathing-related variations were found in the perfusion signals in 14 out of 17 measurements. Breathing has haemodynamic effects [6] and the variations in the perfusion signals may reflect variations in the blood flow. There is, however, a possibility that these variations are motion-related, either due to deformation of the heart caused by the breathing or due to variations in cardiac contraction strength [7,8].

In order to achieve a better understanding of how the perfusion signals are related to the breathing, a study that included measurements of the breathing and blood pressure was performed. This study comprises intra-operative as well as postoperative measurements. In this paper the intra-operative measurements are analyzed. The aim was to investigate the occurrence of breathing-related variations in the perfusion signals and, when occurring, determine the phase delays between the perfusion signals, the blood pressure and the heart rate.

2. Methods

Measurements were performed on twelve patients during CABG surgery. All patients gave informed consent and the study was approved by the regional Human Ethics Committee (No. M117-05).

Before the measurements were completed, the probe came loose from the myocardium on two patients and could not be attached again. No data were available from these patients and therefore they were excluded from the analysis.

The ten patients included in the analysis were denoted A–J. They had a median age of 66.5 years (range 57–82). Eight were men and two were women.

2.1. Laser Doppler system

The measurement system comprises an analog LDPM device (HeNe, 632.8 nm, 2 mW), an intramuscular fibre-optic probe (core/cladding Ø 110/125 µm, fibre separation ≈ 250 µm, probe tip Ø 0.6 mm) and a PC with software for signal processing (LabVIEW®, National Instruments Inc., USA). The LDPM device outputs two signals: perfusion and total backscattered light intensity (DC signal). The system has an upper band limit of 16 kHz and the time constant is 30 ms. Noise compensation is performed in the software.

In order to measure perfusion when tissue motion is small, simultaneous acquisition of the ECG is required. Tissue motion has been found to be at a minimum in late systole and late diastole, i.e., close to the T and P peaks in the ECG [2]. Therefore, the T and P peaks are identified and two perfusion values are calculated as averages over an interval of 10 ms, starting 20 ms before the respective peak. The two perfusion values obtained for each

heartbeat (RR-interval), are denoted PLS (late systole) and PLD (late diastole).

2.2. Measurement protocol

All patients underwent ordinary CABG surgery (one patient also had an aortic valve replacement). Extracorporeal circulation (ECC) was used in all cases. A further description of the surgical procedure is given in [5].

Before, or shortly after, weaning from ECC, the probe was inserted 3–5 mm into the left ventricular wall and fixed with sutures. The perfusion measurement started when the ECC was stopped and the heart was beating normally. During the measurement the patient was mechanically ventilated with the chest still open. In addition to the perfusion and the DC signals, also the ECG, the peripheral arterial blood pressure and the capnography (breathing) signal taken from the patient monitor (CMS, Philips, The Netherlands) were sampled and stored on a computer. At least five minutes of data were recorded from each patient.

This study was part of another study and the probe was therefore left in the myocardium for further measurements after the chest was closed.

2.3. Data analysis

Two sequences of data from each patient were selected for analysis. The sequences had to fulfill the following criteria:

- 6–7 breathing cycles.
- Stable perfusion signals.
- Heart rate variations < 4%.
- Detectable T and P peaks in the ECG.
- Constant ventilator frequency.
- No obvious disturbances in any of the signals.

The automatically detected T and P peaks in the ECGs were manually inspected and, if needed, corrected. PLS and PLD were then calculated as described above. For each RR-interval the instantaneous heart rate (HR), the mean arterial pressure (MAP) and the mean capnography signal were also calculated, after being corrected for time delays in the patient monitor.

Frequency spectrums of all signals were estimated by the periodogram method, including detrending and zero-padding of the data. The spectrums were normalized so that the maximum peak in each signal was 1. The respiration frequency f_{Resp} in each sequence was determined from the maximum peak in the capnography spectrum. Any signal that had a peak of at least 0.5 in the frequency interval of f_{Resp} ± 0.015 Hz was classified as having a breathing-related component.

All signals that had breathing-related variations were then bandpass-filtered around the breathing frequency, using a third order zero-phase Butterworth filter with a bandwidth of 0.05 Hz. In order to determine the phase delays between the signals, the cross-correlation functions for all combinations (PLS-MAP, PLS-HR, PLS-PLD, PLD-MAP, PLD-HR and HR-MAP) of the filtered signals in each sequence were estimated. The cross-correlation sequences were interpolated with a factor of 10 before the phase delays were calculated.

For each signal pair, the mean phase delay vector M was calculated and the distribution of the delays was tested with Rayleigh's test for circular uniformity. A p-value of 0.05 was considered significant.

All calculations were made using MATLAB® (Mathworks Inc, USA).

3. Results

Two data sequences that fulfilled the analysis criteria could be found for each patient. In three cases an atrial pacemaker was used (C-1, C-2 and D-1). Mean heart rate and respiration frequency, as well as presence of breathing-related variations in heart rate, mean arterial pressure and perfusion signals for all sequences, are given in Table 1.

Table 1: Heart rate (HR), respiration frequency (Resp) and presence (x) of breathing-related variations in heart rate (HR), mean arterial pressure (MAP) and perfusion signal in late systole (PLS) and late diastole (PLD).

Subj./ seq.	Mean HR min^{-1}	Resp. min^{-1}	Breathing-related variations			
			HR	MAP	PLS	PLD
A-1	64	20	-	-	-	x
A-2	63	20	x	-	x	x
B-1	59	15	x	x	-	x
B-2	61	15	x	x	x	x
C-1	71	15	x	x	-	-
C-2	72	15	x	x	x	x
D-1	68	15	x	x	x	-
D-2	73	15	x	x	-	x
E-1	58	15	x	x	x	-
E-2	57	20	x	-	-	x
F-1	61	16	x	x	x	x
F-2	61	16	x	x	x	x
G-1	62	15	x	x	x	x
G-2	62	15	x	x	x	x
H-1	90	18	x	x	x	x
H-2	91	18	x	x	-	x
I-1	61	17	x	x	x	-
I-2	66	17	x	x	-	-
J-1	65	20	x	x	-	x
J-2	60	20	x	x	-	-
n			19	17	11	14

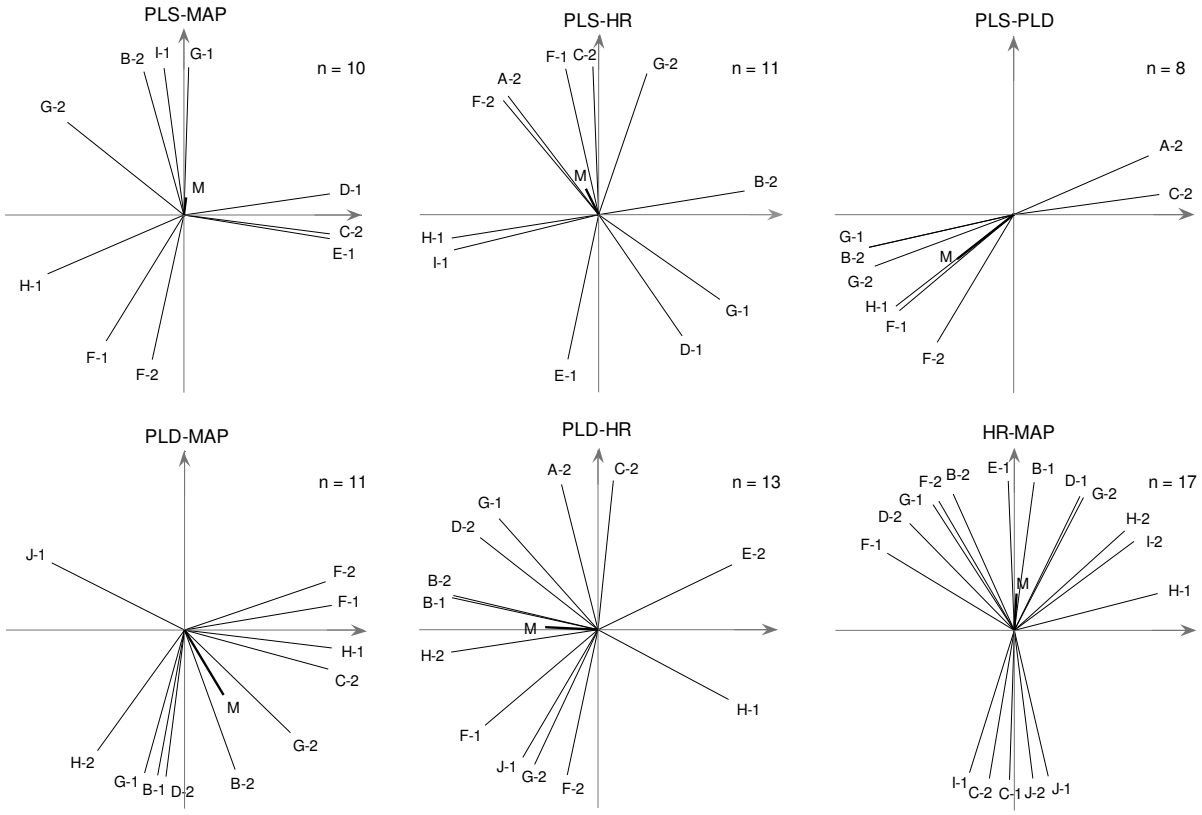

Figure 1: Phase delay distributions. Mean phase delay vectors are marked with an M. When the signal pair S1-S2 has a phase vector in the upper half-plane, S1 precedes S2.

Phase delays (angles) are illustrated as vectors in the unit circle, Figure 1. Mean phase delay vectors are given in Figure 1 and also in Table 2 together with p-values for the uniformity test.

Table 2: Mean phase delay vectors (length and angle) and p-values for the uniformity test.

Signal Pair (S1-S2)	n	Mean length	Mean angle	p-value
PLS-MAP	10	0.12	81	<0.9
PLS-HR	11	0.19	117	<0.7
PLS-PLD	8	0.48	-142	<0.2
PLD-MAP	11	0.51	-59	<0.06
PLD-HR	13	0.36	178	<0.2
HR-MAP	17	0.25	85	<0.4

None of the signal pairs had phase delay distributions that were significantly clumped at a p-level of 0.05. However, Figure 1 indicates a clumping tendency in some of the signal pairs. The distribution of the PLD-MAP vectors has a p-value just above 0.05 and MAP tends to be in phase with, or precede, PLD. HR and PLD tend to be in antiphase, but the spread is large. The phase vectors for HR-MAP are clumped in two directions, where most vectors are in the upper half-plane, i.e., HR precedes MAP. For the signal pairs containing PLS no clear tendencies can be seen.

4. Discussion and conclusions

Breathing-related variations in PLS and PLD were found in more than half of the measurements (11 respective 14 out of 20). The relation between breathing, i.e., inspiration and expiration, and PLS and PLD could not be determined from the capnography signal, since it is not that exact and also has a significant delay. However, this relation can be investigated indirectly from MAP and HR. During positive pressure ventilation, respiratory sinus arrhythmia is reversed, i.e. the heart rate decreases during inspiration [9]. Also, the relation between arterial blood pressure and breathing is reversed, resulting in an inspiratory increase in blood pressure [10,11]. By applying these relations to the PLD-MAP and PLD-HR phase delay distributions in Figure 1, PLD is found to be at a maximum approximately at the end of inspiration or at the beginning of expiration.

To our knowledge, no results have been published

about breathing-related variations in myocardial microcirculation. However, for mechanically ventilated patients, left ventricular stroke volume has been found to be the largest at the end of the inspiratory phase [12]. This could indicate that the variations in PLD are associated with variations in blood flow but, on the other hand, it does not exclude the possibility that the variations are related to tissue motion.

The phase delay distributions of PLS had larger spreads than those of PLD. The amount of data is small though and further analysis is required to confirm the results obtained in this study.

Heart rate precedes mean arterial pressure in 12 out of 17 cases. The five remaining cases could possibly be explained by the breathing-induced rotation of the heart and its electrical axis, which causes heart rate variations in the ECG registration even in the absence of respiratory sinus arrhythmia [13]. This hypothesis is strengthened by the fact that a pacemaker was used in two of the five cases.

The choice of method to determine the presence of breathing-related variations may have an influence on the result. The periodogram method has limitations (see e.g., [14]) and the choice of threshold level and frequency interval directly determines what signals to classify as having breathing-related components. For the data sequences analysed in this study the breathing-related peaks found in the periodogram (i.e., peaks within $f_{Resp} \pm 0.015$ and with an amplitude > 0.5) do correspond rather well with oscillations seen in the time series.

This study is a first step towards better understanding of how PLS and PLD are related to blood pressure, heart rate and to some extent breathing. It has given us knowledge about the phase delays between the signals, but no conclusions can be drawn about the source of the breathing-related variations in PLS and PLD.

Future work will involve analysis of data from postoperative measurements, to further investigate the relations between the perfusion signals and other physiological parameters.

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