

J. Perinat. Med.  
16 (1988) 299

## The first derivative as a means of synchronizing pulsatile flow velocity and vessel diameter waveforms in the fetal descending aorta

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### 1 Introduction

It has become increasingly clear that measurements of blood flow velocity and in particular the vessel diameter for estimating volume flow in the fetal descending aorta, are subject to a number of inaccuracies [1, 6].

One of the important factors in the study of arterial volume flow is the pulsatility of both the flow velocity and vessel diameter profiles. Simultaneous recording of these profiles would allow the construction of a volume flow waveform which takes the pulsatile character of the vessel diameter into account. This is impossible due to unacceptable interference between emitted pulses from real-time and Doppler transducers. An indirect solution to the problem is to compare blood flow velocity and pulsatile vessel diameter profiles in cardiac cycles of similar length as determined by the fetal ECG [3, 5].

An optimal fetal ECG recording cannot always be obtained, even with present day fetal heart rate monitors. Accordingly, we looked for an alternative method of synchronizing pulsatile blood flow velocity and vessel diameter waveforms in the fetal descending aorta that was not dependent on obtaining a fetal ECG. The onset of both waveforms is almost simultaneous [3]. This information was applied to synchronize the two waveforms. To determine the onset of the cardiac cycles the first derivative of the blood flow velocity and pulsatile vessel diameter waveforms was used.

This paper presents (i) a comparative study, where volume blood flow data obtained from the lower thoracic level of the fetal descending aorta was

analyzed initially by the original fetal ECG method [5], and, secondly, re-analyzed using the alternative method in which the first derivative is used for synchronization; (ii) preliminary data on volume flow in the fetal descending aorta in normal third trimester pregnancies using the first derivative method.

### 2 Material and methods

The comparative study was performed in a fetal lamb at 130 days (0.9) of gestation in the first instance. After induction of anesthesia with ketamine hydrochloride (1000 mg), atropine (0.5 mg) and pentobarbital sodium (300 mg) intravenously, the ewe was intubated. An abdominal midline incision was made and the pregnant uterus was subsequently exposed. Throughout surgery the ewe was ventilated with a mixture of nitrous oxide (4:1) and oxygen (2:1) supplemented by enflurane (0.5–2 vol%).

In the second instance, the study was performed in a normal, non smoking human gravida of 37 weeks gestation (0.9), in a semi-recumbent position.

In both the fetal lamb and human fetus, the following three physiological signals were obtained:

- the pulsatile blood flow velocity waveform in the fetal descending aorta using a 2 MHz pulsed Doppler system (PEDOF) attached to a 3.12 MHz linear array real-time transducer (Organon Teknika). In the fetal lamb the real-time transducer was placed directly on the uterine wall.

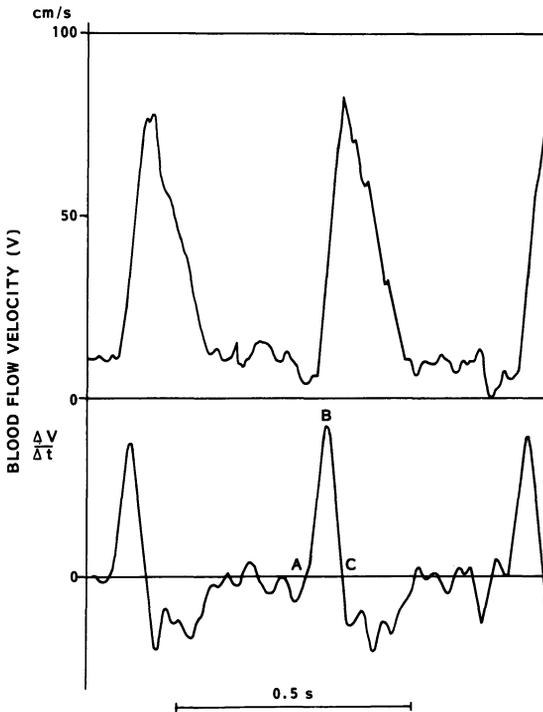
- the pulsatile vessel diameter waveform in the fetal descending aorta using a dual time-distance (TD) recorder. From the real-time image (Organon-Teknika) a line was selected and the markers of the TD recorder were positioned on the deflections of the A-mode representation of the proximal and distal vessel wall.
- the fetal ECG by means of an abdominal ECG monitor (HP-8040). From the maternal abdominal wall in the human study and from electrodes placed in the fetal hind legs in the lamb study. In the analogue output of the ECG monitor a block-shaped pulse indicated the R-top of the fetal ECG.

An Apple II microcomputer was used for data collection following analogue/digital conversion (AI 13, Interactive Structures Inc). All analogue signals were sampled for a fixed period of five seconds at a frequency of 200 Hz, resulting in 1000

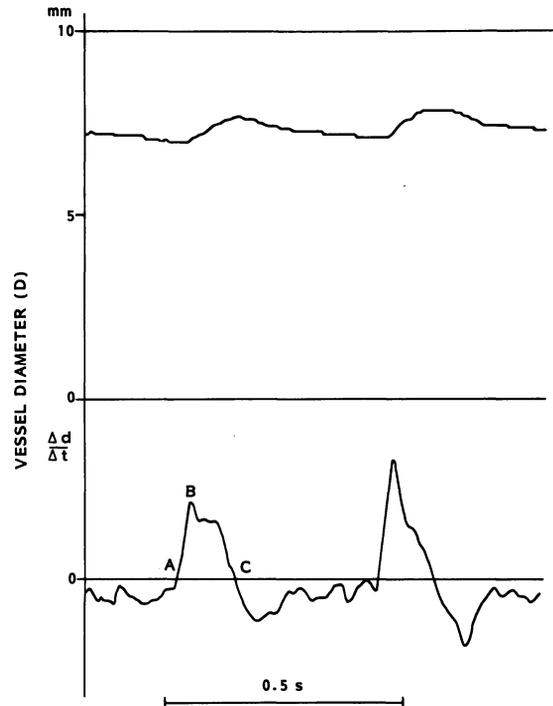
samples for each signal and thus allowing a detailed description of each signal (figures 1 and 2). In the first derivative method, a rise in the upstroke of  $750 \text{ cm s}^{-2}$  for the blood flow velocity profile and of  $6 \text{ mm s}^{-1}$  for the pulsatile vessel diameter profile was arbitrarily selected for accepting a particular cardiac cycle (figures 1 and 2). The maximum rate of rise of the blood flow velocity and pulsatile vessel diameter waveforms was calculated as the peak (B) in the first derivative.

The zero-line crossing (A) preceding this peak was defined as the onset, the zero-line crossing (C) following the peak as the location of the peak in the original blood flow velocity and pulsatile vessel diameter waveforms.

Initially, matching of the blood flow velocity and pulsatile diameter waveforms was carried-out using the R-R intervals of the fetal ECG. A difference in cardiac cycle length of 5% was the maxi-



**Figure 1.** First derivative of the blood flow velocity waveform. A = onset of cardiac cycle; B = point of maximum rise in the waveform; C = peak velocity.



**Figure 2.** First derivative of the pulsatile vessel diameter waveform. A = onset of cardiac cycle; B = point of maximum rate of rise of the waveform; C = maximum diameter.

imum tolerated discrepancy permitted for synchronization of the two waveforms. The following parameters were calculated:

- the pulsatile flow velocity waveform: lagtime between R-top fetal ECG and onset flow velocity (ms), period time (ms), crest time (ms) = time interval between onset and peak velocity, velocity acceleration ( $\text{cm s}^{-2}$ ), peak and end-diastolic velocities ( $\text{cm s}^{-1}$ ), averaged velocity ( $\text{cm s}^{-1}$ ) and pulsatility index [2].
- the pulsatile vessel diameter waveform: lagtime between R-top fetal ECG and onset diameter waveform (ms), period time (ms), crest time (ms), expansion velocity ( $\text{mm s}^{-1}$ ), maximum and minimum diameters (mm) and averaged diameter (mm).
- the volume flow profile: peak flow ( $\text{ml min}^{-1}$ ), aortic stroke volume (ml), averaged volume flow ( $\text{ml min}^{-1}$ ).

In the fetal lamb, a total of 33 cardiac cycles was matched. In the human fetus, the total was 10.

Having completed analysis using the fetal ECG, cardiac cycles were resynchronized applying the first derivative method. The cardiac cycles were matching using onset-to-onset intervals, and the same parameters were calculated. For the fetal lamb, the selected velocity cycles were the same as those utilized for the fetal ECG matching. The computer selected, however, only 25 of the same diameter cycles that were utilized in the fetal ECG synchronization. Similarly, for the human fetus, the velocity cycles were the same. The computer selected only 5 of the same diameter cycles that were utilized for the fetal ECG matching. The diameter cycles used for the first derivative synchronization only were those cardiac cycles that were found to fit the criterium described earlier, where there was a 5% or less difference in cardiac cycle length.

**Table I.** Blood flow velocity, pulsatile vessel diameter and volume flow data at the lower thoracic level for the fetal descending aorta according to fetal ECG (FECG) and first derivative synchronized cardiac cycles in the fetal lamb

	According to FECG		According to first derivative method		% Difference
	X	SD	X	SD	
<b>Velocity cycles</b>					
Lagtime R-top FECG/onset FVWF (ms)	54	9	—	—	—
Crest time (ms)	84	12.5	84	12.5	0.0
Period time (ms)	308	25	305	24	- 1.0
Peak velocity ( $\text{cm s}^{-1}$ )	55.7	9.9	55.7	9.9	0.0
End diastolic velocity ( $\text{cm s}^{-1}$ )	9.4	3.8	3.9	9.8	-58.5
Averaged velocity ( $\text{cm s}^{-1}$ )	23.7	6.8	23.6	7.0	- 0.4
Pulsatility index	2.0	0.3	2.4	0.8	20.0
Velocity acceleration ( $\text{cm s}^{-2}$ )	1112	170	1112	170	0.0
<b>Diameter cycles</b>					
Lagtime R-top FECG/onset VDWF (ms)	50	24	—	—	—
Crest time (ms)	113	22	116	18	- 2.7
Period time (ms)	300	30	309	27	3.0
Maximum diameter (mm)	7.5	0.4	7.5	0.4	0.0
Minimum diameter (mm)	7.2	0.5	6.7	0.4	- 6.9
Averaged diameter (mm)	7.3	0.4	7.2	0.4	- 1.4
Expansion velocity ( $\text{cm s}^{-1}$ )	8.9	2.3	8.8	2.4	- 1.1
<b>Calculated volume flow cycles</b>					
Averaged flow ( $\text{ml min}^{-1}$ )	581	110	575	117	- 1.0
Aortic stroke volume (ml)	2.9	0.4	2.9	0.4	0.0
Peak flow ( $\text{ml min}^{-1}$ )	1439	130	1431	139	- 0.6

FVWF = flow velocity waveform; VDWF = vessel diameter waveform.

A total of 18 patients with normal singleton pregnancies between 30 and 41 weeks of gestation consented to participate in the study. The gestational age had been calculated from a reliable menstrual history and early ultrasonic measurement of fetal crown-rump length or biparietal diameter. Nine patients were between 30 and 35 weeks gestation, and nine patients were between 36 and 41 weeks gestation.

Statistical analysis was performed using the paired student's t-test.

### 3 Results

Tables I and II present the data on blood flow velocity, pulsatile vessel diameter and volume flow (mean  $\pm$  SD) calculated from the waveforms in the fetal lamb and human fetus. According to the fetal ECG synchronization, for the fetal lamb, the lagtime between the R-top fetal ECG and the onset of the blood flow velocity cardiac cycles was

54 ms; whereas, the lagtime between the R-top fetal ECG and the onset of the pulsatile vessel diameter cardiac cycles was 50 ms. This is a difference of  $-4 \pm 29$  (SD) ms. Likewise, for the human fetus, this difference was  $+6 \pm 13$  (SD) ms. These differences are not statistically significant.

The percentage differences in end-diastolic velocities for the fetal lamb and human fetus between the first derivative synchronization and fetal ECG synchronization were  $-58.5$  and  $-53.1$  respectively. These are statistically significant values ( $p < 0.01$ ). The pulsatility index value was therefore significantly higher in the fetal ECG cardiac cycles ( $p < 0.01$ ). The percentage differences in minimum diameter for the fetal lamb and human fetus between both methods of matching were also statistically significant ( $p < 0.01$ ). There was no statistically significant difference found for any of the other parameters, including volume flow calculations.

**Table II.** Blood flow velocity, pulsatile vessel diameter and volume flow data at the lower thoracic level of the fetal descending aorta according to fetal ECG (FECCG) and first derivative synchronized cardiac cycles in the human fetus

	According to FECCG		According to first derivative method		% Difference
	X	SD	X	SD	
<b>Velocity cycles</b>					
Lagtime R-top FECCG/onset FVWF (ms)	46	12	—	—	—
Crest time (ms)	85	15	85	15	0.0
Period time (ms)	431	7	432	17	0.2
Peak velocity ( $\text{cm s}^{-1}$ )	73.1	3.7	73.1	3.7	0.0
End diastolic velocity ( $\text{cm}^{-1}$ )	9.6	2.3	4.5	2.1	$-53.1$
Averaged velocity ( $\text{cm s}^{-1}$ )	24.2	2.4	24.1	2.5	$-0.4$
Pulsatility index	2.6	0.2	2.9	0.3	11.5
Velocity acceleration ( $\text{cm s}^{-2}$ )	1673	194	1673	194	0.0
<b>Diameter cycles</b>					
Lagtime R-top FECCG/onset VDWF (ms)	52	6	—	—	—
Crest time (ms)	118	12	125	11	5.9
Period time (ms)	431	7.4	437	13	1.4
Maximum diameter (mm)	8	0.5	8.1	0.6	1.3
Minimum diameter (mm)	7.6	0.5	7.4	0.5	$-2.6$
Averaged diameter (mm)	7.8	0.5	7.7	0.5	$-1.3$
Expansion velocity ( $\text{cm s}^{-1}$ )	9.7	2.1	8.9	0.6	$-8.2$
<b>Calculated volume flow cycles</b>					
Averaged flow ( $\text{ml min}^{-1}$ )	729	143	701	130	$-3.7$
Aortic stroke volume (ml)	5.2	1.0	5.1	1.0	$-1.9$
Peak flow ( $\text{ml min}^{-1}$ )	2254	315	2196	327	$-2.6$

FVWF = flow velocity waveform; VDWF = vessel diameter waveform.

In the preliminary clinical study averaged mean blood flow (ml/min) was  $396.4 \pm 60.0$  (SD) between 30 and 35 weeks and  $618.9 \pm 76.0$  (SD) between 36 and 41 weeks. This difference was statistically significant ( $p < 0.0005$ ).

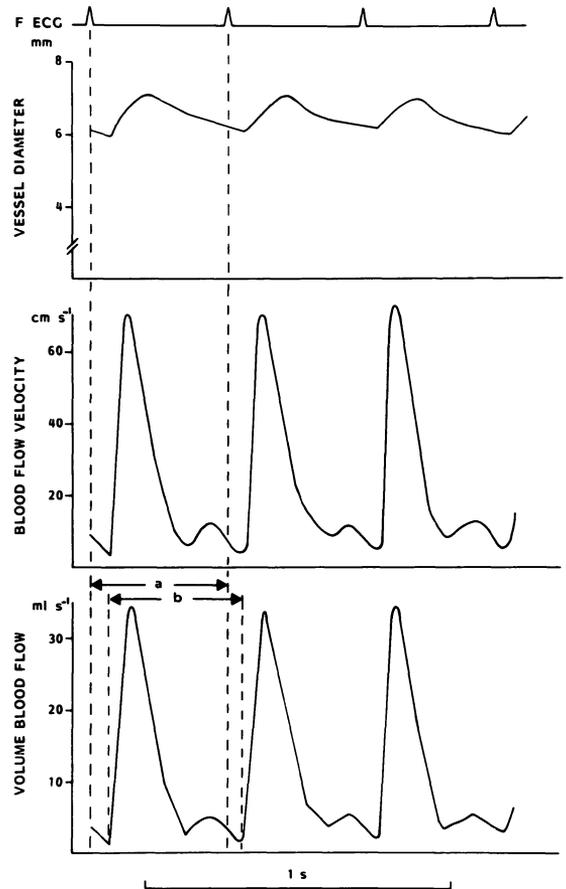
#### 4 Discussion

The present study shows a good agreement between fetal ECG and "first derivative" synchronized cardiac cycles with respect to nearly all blood flow velocity and pulsatile vessel diameter parameters both in the fetal lamb and human fetus.

Both in the fetal lamb and human fetus, the mean time lag between the onset of the blood flow velocity and pulsatile vessel diameter waveforms appeared to be negligible (4 and 6 msec), so that the onset of both waveforms can be considered as being simultaneous. This is in agreement with other studies [3, 4]. The significant difference in end-diastolic flow velocity and minimum vessel diameter between the two methods of synchronization is determined by artificially increased end-diastolic flow velocity and minimum vessel diameter values using the fetal ECG. This is due to the lagtime between the R-top of the fetal ECG and onset of both waveforms (figure 3). In other words, the cardiac cycles of the fetal ECG precede the cardiac cycles of the blood flow velocity and pulsatile vessel diameter waveforms (figure 3). It can be concluded that the first derivative method is a satisfactory replacement to the fetal ECG as a means of synchronizing blood flow velocity and pulsatile vessel diameter waveforms in the fetal descending aorta. Its easy applicability offers an attractive alternative to the fetal ECG. It will serve as a useful tool on further comparative studies on pulsatile changes in human fetal aortic flow velocity and vessel diameter waveforms both under physiological and pathophysiological circumstances.

#### Abstract

In order to calculate volume flow, blood flow velocity and pulsatile vessel diameter waveforms in the lower thoracic part of the descending aorta of the fetal lamb and human fetus were matched for identical cardiac cycle length by fetal ECG and the first derivative of these waveforms. Volume flow values were not essen-



**Figure 3.** The synchronization of the pulsatile vessel diameter and blood flow velocity waveforms by fetal ECG, from which volume blood flow waveforms can be constructed. (a-b) = lagtime between fetal ECG and onset of the cardiac cycles for all waveforms.

tially different using either method. There is simultaneous onset of the blood flow velocity and pulsatile vessel diameter waveforms. The first derivative can reliably replace the fetal ECG as a means of synchronizing blood flow velocity and pulsatile vessel diameter waveforms in the fetal descending aorta.

**Keywords:** Aortic diameter, aortic flow velocity, fetal blood flow, pulsed Doppler.

### Zusammenfassung

#### Die erste Ableitung der pulsatilen Flußkurve der Aorta des. als Mittel zur Synchronisation der Geschwindigkeits- und der Gefäßdurchmesserkurve

Um das Flußvolumen, die Blutflußgeschwindigkeit und den pulsierenden Gefäßdurchmesser im unteren Thoraxanteil der Aorta des. im Lammfeten und im menschlichen Feten berechnen zu können, wurden über das fetale EKG die Pulse zu gleichen Herzzyklen bestimmt und

die zugehörigen ersten Ableitungen dieser Wellenformen gebildet. Der Beginn der Blutflußgeschwindigkeit und der des pulsatilen Gefäßdurchmessers ist gleich. Die erste Ableitung kann zuverlässig das fetale EKG als Mittel zur Synchronisation der Wellen der Flußgeschwindigkeit und des pulsierenden Gefäßdurchmessers in der fetalen Aorta des. ersetzen.

**Schlüsselwörter:** Aortendurchmesser, fetaler Blutfluß, Flußgeschwindigkeit in der Aorta, gepulster Doppler.

### Résumé

#### La première dérivée: moyen de synchronisation de la vélocité du flux sanguin et des ondes pulsatiles du diamètre des vaisseaux au niveau de l'aorte descendante du fœtus

Afin de calculer le débit, la vélocité du flux sanguin et les ondes pulsatiles du diamètre des vaisseaux au niveau de la portion thoracique inférieure de l'aorte descendante du fœtus d'agneau et du fœtus humain, ont été apparées quant à la longueur identique du cycle cardiaque sur l'ECG fœtal et la première dérivée de ces ondes. Les

valeurs du débit ne sont pas notablement différentes quelle que soit la méthode. La vélocité du flux sanguin et les ondes pulsatiles du diamètre des vaisseaux débutent simultanément. La première dérivée peut remplacer de façon fiable l'ECG fœtal comme moyen de synchronisation de la vélocité du flux sanguin et des ondes pulsatiles du diamètre des vaisseaux au niveau de l'aorte fœtale descendante.

**Mots-clés:** Débit sanguin fœtal, diamètre aortique, doppler pulsé, vélocité du flux aortique.

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