BEAT-TO-BEAT COMPUTATION OF FETAL CARDIAC TIME INTERVALS FROM FMCG: COMPARISON WITH ESTIMATES ON AVERAGED CARDIAC CYCLES

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Abstract: Fetal magnetocardiography (fMCG) allows the non-invasive registration of fetal cardiac activity. By means of independent component analysis (ICA) it is possible to process fMCG recordings in order to reconstruct reliable fetal cardiac traces on which fetal cardiac time intervals (fCTI) can be evaluated to help assessing the fetal heart function. In this paper, we studied the duration of the P wave, PQ interval, QRS complex, ST interval and T wave, which were evaluated with a beat-to-beat analysis of the fetal traces obtained from fMCG datasets recorded in uncomplicated pregnancies. The analysis of several consecutive heart beats on long segments of fetal signals permitted calculating the variability range of each time interval at an intra-individual level. The reliability of this method was assessed with respect to fCTI estimated on the averaged beats obtained from the same rhythm strips used for single cycle analysis.

Introduction

Fetal magnetocardiography (fMCG) has shown to be a promising tool for the detection of fetal heart electrical activity, thus providing gynecologists and neonatologists with traces that can be useful for the antenatal monitoring and diagnostics [1-2].

Several studies have validated the reliability of fetal magnetocardiography for the acquisition of fetal cardiac signals. However, a mandatory condition for the clinical use of fMCG is the reliable extraction of fetal cardiac traces from the recorded magnetocardiograms, which are mixtures of the signals generated from the fetal and maternal hearts simultaneously.

In general, the fetal traces reconstructed from fMCG are precise enough to allow the identification of the beginning and end of P, QRS and T waves, thereby enabling the quantification of fetal cardiac time intervals (fCTI) [3-6]. This information is useful to complement the existing prenatal monitoring techniques in case of fetal cardiac dysfunction such as long QT, ischaemia, arrhythmia and growth retardation [7-13].

FCTI are usually estimated on averaged beats to eliminate residual magnetic noise, to ease the detection of the weak P and T waves, and to reduce the overall processing time; though, the use of averaged beats implies that the physiological variability of fCTI in single fetuses is disregarded, with a consequent loss of information.

In the present study, we employed independent component analysis (ICA) to process fMCG recordings; the reconstructed fetal signals had average signal-to-noise ratio (SNR) values generally between 12 and 18 dB. As a result, P, QRS and T waves could be identified on single cardiac cycles of trace segments long enough to permit not only the quantification of average fCTI, but also of their intra-individual beat-to-beat variability [14]. The reliability of this method was assessed comparing the attained averaged fCTI with those estimated on averaged beats obtained from the same rhythm strips used for single cycle analysis.

Materials and Methods

Fetal magnetocardiograms were acquired by means of a multi-channel MCG system operating in a shielded room for environmental magnetic noise reduction. The system has 55 sensing channels homogeneously arranged on a circular surface inside a cylindrical cryostat [15].

The Ethical Committee of our University approved the study protocol, which consisted in the longitudinal evaluation of 20 singleton uncomplicated pregnancies (maternal age = 32 ± 6 yrs). Each volunteer participated in the study after written informed consent, and she underwent a fMCG acquisition every 4 to 6 weeks, starting from about the 22nd gestational week until delivery for a total of 3 to 4 fMCG sessions.

Each acquisition lasted 5-10 minutes; sampling frequency was 1 kHz, and the signals were converted in digital form and filtered between 0.016 Hz and 250.0 Hz.

FMCG acquisitions provided 55 simultaneous raw traces that included the signals from the fetal and maternal hearts, a signal due to uncontrolled abdominal movements, ambient noise and, eventually, power line contamination. The recording MCG system was

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positioned over the maternal abdomen in order to get as close as possible to the fetal heart, the position of which was previously determined by means of ultrasound scan.

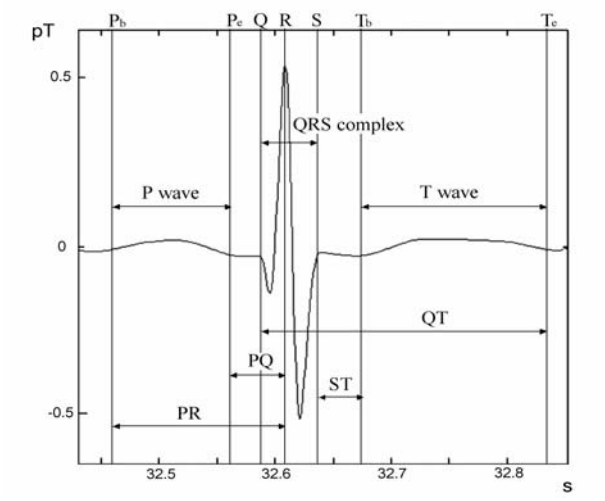

Figure 1: QRS complex, P and T waves and fCTI on a smoothed real-time fetal cardiac cycle. Time is given in seconds from acquisition beginning and signal intensity is measured in pT.

The pre-processing of traces consisted in band-pass filtering between 0.4 and 150 Hz and in suppressing the residual power line disturbance by means of a notch filter at 50 Hz.

FastICA algorithm [16] was used for fetal signal reconstruction. For each dataset, clustering of MCG channels allowed reconstructing 8 simultaneous fetal traces [17-20], which were further smoothed to reduce any residual high-frequency noise.

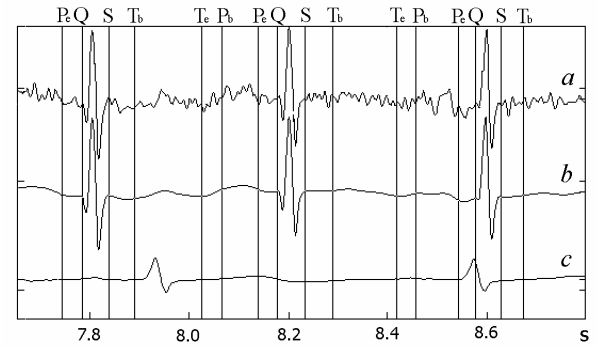

Figure 2: Reconstructed (a) and smoothed fetal traces (b). The simultaneous maternal ECG (c) is provided to show absence of maternal interference in the fetal traces. Vertical lines on subsequent cardiac cycles identify the onset and offset of P, QRS and T waves. Time is given in seconds from acquisition beginning and trace amplitude is in arbitrary units.

For each fMCG session, the reconstructed fetal signals showing the clearest waveform were used to estimate fCTI, with a minimum of three traces; at least 50 consecutive cardiac cycles of each selected fetal signal were included in the analysis. The duration of P and T waves, QRS complex, and PQ and ST intervals was calculated following the standard definitions, reported in Figure 1 for more clarity [21]; ventricular frequency (RR interval) was also determined.

The beginning and end of each wave were identified on all selected beats (Figure 2); their values were automatically stored and used for subsequent analysis.

For each woman and for all acquisition sessions referring to her, intra-individual variability analysis of fCTI was performed. Inter-individual variability analysis of fCTI was completed by grouping the results obtained on single patients in function of gestational age. The total period, ranging from 22 to 37 gestational weeks, was divided in 4 sub-periods of 4 weeks each. For each sub-period and for all intervals we calculated the average and associated sampled standard deviation (SSD), which tskes into account the total number of fetal cycles used to calculate the averages.

In order to compare our results with those obtained by other research groups who estimated fCTI on averaged beats, we calculated fCTI also on the averaged fetal beats obtained from the same rhythm strips used for beat-to-beat analysis. For each time interval and for each gestational sub-period, we calculated an average percent variation between the results of the two methods as

$$\overline{PD} = \frac{1}{N}\sum_{i=1}^{N}\left[\frac{(x_{ai} - \overline{x_{bi}})}{x_{ai}}\right]100 \qquad (1)$$

where i identifies the dataset, N is the total number of data sets belonging to the analyzed sub-period, x_{ai} is the interval duration estimated on averaged beats whereas x_{bi} is the average interval duration estimated on single cycles.

Results

Three women out of the 20 enrolled were excluded from the study because fetal arrhythmias occurred during fMCG. In total, 59 fMCG data sets of 55 recordings each were available for longitudinal analysis from 17 women; a total of more than 3000 fetal cardiac cycles were analyzed (Table 1).

Examples of fCTI analysis calculated on averaged beats and on single cycles are shown in Figure 3 and 4.

The overall detection rate of fetal signals reconstructed with FastICA was very good (93%); its value for early gestation was also remarkable (75%) (Table 1). Beat-to-beat estimates of fCTI on at least 50 consecutive beats were performed on all retrieved traces except two traces (24 and 27 weeks): their poor quality only permitted the calculation of RR interval variability.

The longitudinal charts of normal fCTI for different gestational periods are given in Table 1; they were calculated using the results of intra-individual analysis.

FCTI estimated on both single cycles and averaged beats, and referring to the total population, are shown in Table 2; the percent variations of beat-to-beat estimates with respect to averaged beats estimates are also provided.

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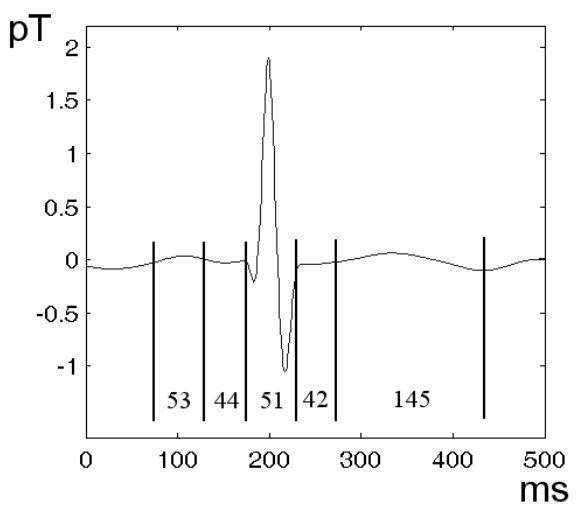

Figure 3: Example of fCTI analysis performed on the average cardiac cycle of a fetus at 36 weeks. Time is given in seconds and amplitude in pT.

Table 1 - Longitudinal charts of normal fCTI along pregnancy; they were calculated with intra-individual beat-to-beat analysis on more than 3000 cardiac cycles and on averaged fetal beats. Averages and related standard deviations, given in parentheses, are expressed in ms. Figures referring to averaged beats are given without variability estimates for each gestational period.

		Gestational sub-periods (weeks)			
		22 - 25	*26 - 29*	*30 - 33*	*34 - 37*
fMCG datasets		12	16	15	16
reconstructed fetal sets		9 (75%)	15 (94%)	15 (100%)	16 (100%)
*RR interval**		406 (10)	432 (14)	436 (10)	437 (16)
P wave	*Single cycles*	50 (8)	54 (9)	51 (7)	55 (6)
	Averaged beat	53	62	58	59
PQ	*Single cycles*	49 (8)	52 (8)	48 (7)	52 (7)
	Averaged beat	47	47	46	50
QRS	*Single cycles*	54 (5)	54 (5)	53 (5)	58 (4)
	Averaged beat	52	55	54	57
ST	*Single cycles*	56 (3)	58 (4)	54 (4)	57 (4)
	Averaged beat	60	60	65	63
T wave	*Single cycles*	141 (6)	146 (8)	135 (6)	147 (9)
	Averaged beat	128	133	127	135

* average value (SD) estimated with beat-to-beat analysis

Discussion

We have demonstrated in previous works [17-20] that FastICA permits the reconstruction of reliable fetal traces in a large number of cases (Table 1); fetal signals show a dependable morphology, so that fCTI could be assessed on single cardiac cycles. The availability of clear and stable fetal signals allowed calculating fCTI on a high number of consecutive beats with a precision increase (Table 1) and the possibility to estimate, for each time interval, its intra-individual variability, which provides information amenable to be lost when fCTI are assessed on averaged traces.

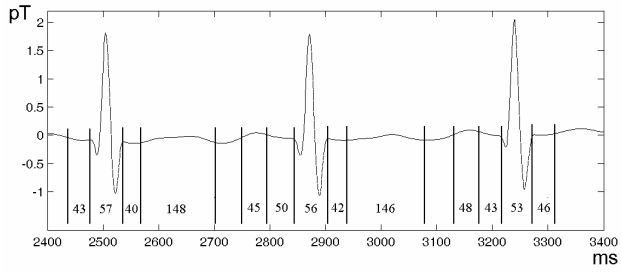

Figure 4: Example of fCTI analysis performed on single cycles, for the same fetus of Figure 3. Time is given in seconds and amplitude in pT.

Table 2 - fCTI estimated from beat-to-beat analysis and on averaged beats. Averages and related standard deviations, given in parentheses, are expressed in ms. Figures refer to the total population. Average percent differences between fCTI calculated with the two approaches are provided in the last column.

	Single cycles	*Averaged beat*	*% variation*
P wave	53 (8)	59	- 10.2
PQ	50 (7)	48	+ 4.2
QRS	55 (5)	55	+ 0.4
ST	56 (4)	63	- 11.1
T wave	142 (7)	134	+ 6.0
*RR**	428 (14)		

* RR interval only estimated with beat-to-beat analysis

Percent differences between fCTI obtained with the two methods were negligible for QRS complex, whereas they became more important for intervals, in particular for P and T wave, which were underestimated and overestimated with respect to the averaged beat estimates.

When comparing the outcome of our study with normality data developed cross-sectionally from a large population of women evaluated only once in their pregnancy [3-6], a general agreement with the results by Grimm et al. [3] and Lowery et al. [6] was found, whereas some differences with those found by Stinstra et al. [4] and Van Leeuwen et al. [5] were detected. Remarkably, the differences between those findings and our results diminished when the comparison was performed with fCTI estimated on averaged beats.

Since the same rhythm strips were used to estimate fCTI on single cycles and averaged beats, it is possible to ascribe the observed differences to the averaging procedure. In fact, the physiological variability of fetal heart rate implies that the length of a cardiac wave may change in subsequent beats, inducing, in the averaged signal, an error that may increase with its distance from the alignment point (R peak).

Residual differences may be due, as claimed by Burgoff et al. [22], to factors related to fetal behavioural

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state, position and orientation during fMCG, to the type and number of magnetic sensors used, and to environmental noise: those conditions may induce important errors, of up to several milliseconds, in fCTI estimates. However, since those errors are expected to be normally distributed, we may argue that their contribution to the observed differences in fCTI estimates should be negligible. On the other hand, fetal cardiac signals restored with FastICA showed to be independent on sensors configuration (Figure 2) and unaffected by fetal movements, which were separated and disregarded as all other noise components.

Conclusion

The availability of stable high SNR fetal signals allowed calculating fCTI on sequences of beats with increased precision, and estimating their physiological variability within single subjects. Conversely, this information is unavoidably lost when fCTI are assessed on averaged beats, procedure that may also induce important errors in the estimation of fCTI related to the weak P and T waves.

References

[1] PETERS M., CROWE J., PIERI J.F., QUARTERO H., HAYES-GILL B., JAMES D., STINSTRA J. and SHAKESPEARE S. (2001): "Monitoring the fetal heart non-invasively: a review of methods." *J Perinat Med*, **29**, pp. 408-416

[2] LEWIS MJ. (2003): "Review of electromagnetic source investigations of the fetal heart" *Med Eng Phys*, **25**, pp. 801-810

[3] GRIMM B., KÄHLER C., SCHLEUSSNER E., SCHNEIDER U., HAUEISEN J. and SEEWALD H.J. (2003): "Influence of intrauterine growth restriction on cardiac time intervals evaluated by fetal magnetocardiography" *Early Hum Dev*, **74**, pp. 1-11

[4] STINSTRA J., GOLBACH E., VAN LEEUWEN P., LANGE S., MENENDEZ T., MOSHAGE W., SCHLEUSSNER E., KAEHLER C., HORIGOME H., SHIGEMITSU S. and PETERS MJ. (2002): "Multicentre study of fetal cardiac time intervals using magnetocardiography" *Brit J Obstr Gynecol*, **109**, pp. 1235-1243

[5] VAN LEEUWEN P., LANGE S., KLEIN A., GEUE D., ZHANG Y., KRAUSE H.J. and GRONEMEYER D. (2004): "Reproducibility and reliability of fetal cardiac time intervals using magnetocardiography" *Physiol Meas*, **25**, pp. 539-552

[6] LOWERY C.L., CAMPBELL J.Q., WILSON J.D., MURPHY P., PREISSL H., MALAK S.F. and ESWARAN H. (2003): "Noninvasive antepartum recording of fetal S-T segment with a newly developed 151-channel magnetic sensor system" *Am J Obstet Gynecol*, **188**, pp. 1491-1497

[7] MENENDEZ T., ACHENBACH S., BEINDER E., HOFBECK M., SCHMID O., SINGER H., MOSHAGE W. and DANIEL W.G. (2000): "Prenatal diagnosis of QT prolongation by magnetocardiography", *Pacing Clin Electrophysiol*, **23**, pp. 1305-1307

[8] HOSONO T., KANEGAWA T., CHIBA Y., KANDORI A. and TSUKADA K. (2002): "The coincidence of fetal magnetocardiography and direct electrocardiography in a case of fetal atrial flutter due to intracardiac tumor" *Fetal Diagn Ther*, **17**, pp. 331-333

[9] WAKAI R.T., STRASBURGER J.F., LI Z., DEAL B.J. and GOTTEINER N.L. (2003): "Magnetocardiographic rhythm patterns at initiation and termination of fetal supraventricular tachycardia" *Circulation*, **107**, pp. 307-312

[10] VAN LEEUWEN P., HAILER B., BADER W., GEISSLER J., TROWITZSCH E. and GRONEMEYER D.H. (1999): "Magnetocardiography in the diagnosis of fetal arrhythmia" *Br J Obstet Gynaecol* 1999, **106**, pp. 1200-1208

[11] COMANI S., LIBERATI M., MANTINI D., GABRIELE E., BRISINDA D., DI LUZIO S., FENICI R. and ROMANI G.L. (2004): "Characterization of fetal arrhythmias by means of fetal magnetocardiography in three cases of difficult ultrasonographic imaging" *Pacing Clin Electrophysiol*, **27**, pp. 1647-1655

[12] KAHLER C., GRIMM B., SCHLEUSSNER E., SCHNEIDER A., SCHNEIDER U., NOWAK H., VOGT L. and SEEWALD H.J. (2001): "The application of fetal magnetocardiography (FMCG) to investigate fetal arrhythmias and congenital heart defects (CHD)" *Prenat Diag*, **21**, pp. 176-182

[13] HORIGOME H., SHIONO J., SHIGEMITSU S., ASAKA M., MATSUI A., KANDORI A., MIYASHITA T. and TSUKADA K (2001): "Detection of cardiac hypertrophy in the fetus by approximation of the current dipole using magnetocardiography" *Pediatric Research*, **50**, pp. 242-245

[14] COMANI S., LIBERATI M., MANTINI D., MERLINO B., ALLEVA G., GABRIELE E., DI LUZIO S. and ROMANI G.L. (2005): "Beat-to-beat estimate of fetal cardiac time intervals using magnetocardiography: longitudinal charts of normality ranges and individual trends", *Acta Gynecol Obst Scand*, **at press.**

[15] DELLA PENNA S, DEL GRATTA C, ERNE S.N., GRANATA C., PASQUARELLI A., PIZZELLA V., ROSSI R., RUSSO M., TORQUATI K. and ROMANI G.L. (2000): "Biomagnetic systems for clinical use" Philosoph Magaz, **80**, pp. 937-948

[16] HYVÄRINEN A. (1999): "Fast and robust fixed-point algorithms for independent component analysis" *IEEE Trans. on Neural Networks*, **10**, pp. 626-634

[17] MANTINI D, COMANI S, PENNESI P. and CANCELLIERI G. (2004): "Tailoring of the Independent Component Analysis to multi-channel fMCG recordings for an optimal reconstruction of the fetal cardiac signal" *Biomed Tech*, **48**, pp. 186-188

[18] COMANI S., MANTINI D., PENNESI P., LAGATTA A. and CANCELLIERI G. (2004): "Independent component analysis: fetal signal reconstruction

ISSN: 1727-1983

from magnetocardiographic recordings" *Comput Meth Prog Bio*, **75**, pp. 163-177

[19] COMANI S., MANTINI D., LAGATTA A., ESPOSITO F., DI LUZIO S. and ROMANI G.L. (2004): "Time course reconstruction of fetal cardiac signals from fMCG: Independent Component Analysis vs. Adaptive Maternal Beat Subtraction" *Physiol Meas*, **25**, pp. 1305-1321

[20] COMANI S., MANTINI D., ALLEVA G., DI LUZIO S., and ROMANI G.L. (2004): "Fetal Magnetocardiographic Mapping using Independent Component Analysis" *Physiol Meas*, **25**, pp. 1459-1472

[21] GRIMM B., HAUEISEN J., HUOTILAINEN M., LANGE S., VAN LEEUWEN P., MENENDEZ T., PETERS M.J., SCHLEUSSNER E. and SCHNEIDER U. (2003): "Recommended standards for fetal magnetocardiography" *Pacing Clin Electrophysiol*, **26**, pp. 2121-2126

[22] BURGHOFF B., STEINHOFF U., HABERKORN W. and KOCH H. (1997): "Comparability of measurement results obtained with multi-SQUID-systems of different sensor configurations" *IEEE Trans Appl Supercond*, pp. 3465-3468

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