April 4, 2009

Perinatal Biomagnetism 2009:

how can it help sick fetus/infant?

1st International Workshop

on the clinical usefulness of
Biomagnetism in Perinatal Medicine

Chieti, Italy

Ce.S.I. – "G. d'Annunzio" University

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For any question regarding the scientific aspects of the Workshop, please send an email to pb2009@udanet.it

Dear colleagues,

it is our great pleasure to welcome you at **Perinatal Biomagnetism 2009**, the 1st International Workshop on the clinical usefulness of Biomagnetism in Perinatal Medicine.

Perinatal Medicine has gone through an enormous development over the last 50 years, and **Perinatal Biomagnetism 2009** is intended to address critical issues related to the monitoring of fetal and neonatal well-being using Biomagnetism. Disciplines of Biomagnetism are utilized to expand detection and imaging technologies, to investigate biological, physiological and pathological functions, and to develop clinical applications.

The purpose of **Perinatal Biomagnetism 2009** is to provide obstetricians, perinatologists, pediatricians, pediatric neurologists and pediatric cardiologists, who might be interested in new technologies in translational Perinatal Medicine, with an updated overview of the state-of-the-art in the application of Magnetocardiography (MCG) and Magnetoencephalography (MEG) in the specific field of fetal and neonatal medicine. The advantages and disadvantages, and the potential usefulness of these new techniques with respect to other methods used in perinatal surveillance, will be presented and analyzed by specialists coming from all over the world.

We sincerely hope that **Perinatal Biomagnetism 2009** will offer you an opportunity to become more familiar with biomagnetic techniques and to discuss the results of your latest research in Perinatal Medicine, from which future progress might stem.

Silvia Comani and Janette Strasburger

Workshop Chair Persons

Contents

Committees

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Silvia Comani, Chieti (Italy)

Workshop Chair persons:

Silvia Comani, Chieti (Italy)
Janette F. Strasburger, Milwaukee, Wisconsin (USA)

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Invited speakers

F. Chiarelli, M.D., University of Chieti (Italy)

B.F. Cuneo, M.D., Hope Children's Hospital, Oak Lawn, Illinois (USA)

J. Haueisen, Ph.D., Technical University of Ilmenau (Germany)

Y. Okada, Ph.D., University of New Mexico, Albuquerque (USA)

E. Pihko, Ph.D., Helsinki University of Technology, Espoo (Finland)

H. Preissl, Ph.D., University of Tuebingen (Germany) and University of Arkansas Little Rock (USA)

U. Schneider, M.D., Friedrich – Schiller University, Jena (Germany)

J.F. Strasburger, M.D., Medical College of Wisconsin, Milwaukee (USA)

P. van Leeuwen, Ph.D., University of Witten/Herdecke, Bochum (Germany)

R.T. Wakai, Ph.D., University of Wisconsin, Madison (USA)

Chair persons

Silvia Comani, Chieti (Italy)

Bettina F. Cuneo, Oak Lawn, Illinois (USA)

Yoshio Okada, Albuquerque, New Mexico (USA)

Uwe Schneider, Jena (Germany)

Janette F. Strasburger, Milwaukee, Wisconsin (USA)

Peter van Leeuwen, Bochum (Germany)

Final Program

8:30 am – 11:00 am	On site Registration
9:00 am – 9:10 am	**Welcome address**
9:10 am – 10:10 am	**Plenary lectures** Chairs: Silvia Comani and Janette Strasburger
9:10 am – 9:40 am	Biomagnetism in children Francesco Chiarelli M.D., *Chieti (Italy)*
9:40 am – 10:10 am	Biomagnetic measurement techniques Jens Haueisen, Ph.D., *Jena (Germany)*
10:10 am – 11:00 am	Coffee break & Posters
11:00 am – 13:00 pm	**MCG lectures** Chairs: Peter van Leeuwen and Bettina F. Cuneo
11:00 am – 11:30 am	Processing and Analysis of fetal MCG data Peter van Leeuwen, Ph.D., *Bochum (Germany)*
11:30 am – 12:00 pm	What does heart rate variability tell us about the development of autonomic nervous regulation during fetal life? Uwe Schneider, M.D., *Jena (Germany)*
12:00 pm – 12:30 pm	Clinical Usefulness of Fetal MCG in the Diagnosis and Management of the Fetus with, and at risk for, Arrhythmia Bettina F. Cuneo, M.D., *Chicago (Illinois - USA)*
12:30 pm – 13:00 pm	Simultaneous Fetal MCG and Echocardiography Janette F. Strasburger, M.D., *Neenah (Wisconsin - USA)*
13:00 pm – 14:30 pm	Get-together lunch & Poster walk
14:30 pm – 16:30 pm	**MEG lectures** Chairs: Yoshio Okada and Uwe Schneider
14:30 pm – 15:00 pm	Fetal Magnetoencephalography: Extraction of fetal brain signals in the presence of large interfering signal sources Hubert Preissl, Ph.D., *Tuebingen (Germany) and Little Rock (AR - USA)*
15:00 pm – 15:30 pm	Perinatal MEG Ron T. Wakai, Ph.D., *Madison (Wisconsin - USA)*
15:30 pm – 16:00 pm	MEG in neonatology: Somatosensory cortical processing in healthy and at-risk babies Elina Pihko, Ph.D., *Helsinki (Finland)*
16:00 pm – 16:30 pm	Neonatal brain development in patients with brain disorders Yoshio Okada, Ph.D., *Albuquerque (New Mexico - USA)*
16:30 pm – 17:00 pm	Coffee and tea break & Posters
17:00 pm – 18:00 pm	**Round Table** Chairs: Silvia Comani and Janette Strasburger
17:00 pm – 17:10 pm	Biomagnetism in Perinatal Medicine: how can new technologies help sick fetus/infant? Remarks on current Perinatal Clinical Psychology Mario Fulcheri, M.D., *Chieti (Italy)*
18:00 pm – 18:10 pm	**Closing remarks and farewell address**

Plenary lectures

Chair persons:
Silvia Comani and Janette Strasburger

Francesco Chiarelli

Francesco Chiarelli is Professor of Paediatrics at the Department of Paediatrics, University of Chieti, Italy. He received his undergraduate education at the University of Siena, Italy.
His main research interests are in molecular and cellular biology of diabetic angiopathy; in insulin resistance in children; in the early detection of diabetic microangiopathy in children; in obesity and type 2 diabetes in children.
He is author of more than 380 scientific papers on impacted journals, some of which have been published in leading scientific journals such as The Lancet, New England Journal of Medicine, Journal of Clinical Endocrinology and Metabolism, Diabetes, Diabetes Care, Diabetologia, Clinical Endocrinology, Circulation, ATVB.
He is on the Editorial Board of Journal of Pediatric Endocrinology and Metabolism, Pediatric Diabetes, Hormone Research, Diabetes, Nutrition and Metabolism.
He is General Secretary of the European Society of Paediatric Endocrinology (ESPE) for the period 2004-2010 and Member of the WHO Task Force for Childhood Diabetes.
He holds membership in several professional organizations, including the International Society for Pediatric and Adolescent Diabetes (ISPAD) and the American Diabetes Association (ADA).

Biomagnetism in children

Francesco Chiarelli and Alessandra Savino

Department of Pediatrics, University of Chieti, Italy

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Since the introduction (in 1982) of a biomagnetic facility in the clinical environment, efforts were concentrated to investigate whether magnetocardiography (MCG) and magnetoencephalography (MEG) in the specific field of foetal, neonatal and paediatric medicine could provide new information of potential diagnostic use.
These methods have proven to be valuable and non-invasive as research tools in corresponding bioelectric measurements and obtaining functional information that is

difficult to gain by conventional clinical imaging methods, and have now entered routine clinical application.

Emergence of fetal magnetocardiography (fMCG) has made it possible to electrophysiologically evaluate foetal cardiac events. fMCG has been used to detect the foetal cardiac activity at different gestational ages in normal and high risk pregnancies and has progressively shown its potential for the non-invasive monitoring of the foetal heart function and well-being.

fMCG may help to identify congenital heart defects (CHD) (e.g. right heart hypoplasia) and the progression of the disease. Moreover, fMCG seems to be the most reliable tool for prenatal diagnosis of long QT syndrome and can also be used to detect foetal heart rate variability as a marker for neuro-vegetative development in normal and high risk pregnancies. More applications of fMCG in prenatal medicine would improve detection rates and prognosis of congenital arrhythmias (e.g. tachycardia, complex tachy-/bradycardia, ventricular extrasystoles, Wolf-Parkinson-White syndrome). If morphological analysis of PQRST waveforms using fMCG is combined, much more useful information for prenatal diagnosis and management of channelopathies could be obtained, and choosing an antiarrhythmic agent based on those results could make treatment more effective. fMCG is also useful for detailed analysis of electrophysiological properties of congenital AVB. Prognosis of a foetuses with complete AVB is rather dim without cardiac pacing.

MEG is a new powerful tool for noninvasively measurement neuromagnetic signals originating from the brain. Since MEG can detect neuromagnetic signals with high spatial and temporal resolution, many brain properties can be studied. In children MEG may be useful in evaluating non-invasively the functionalities of the sensori-motor, auditory, visual, and language systems during normal maturation. Furthermore, MEG could help in identifying abnormalities in neurological or neurodevelopmental disorders. In addition, MEG can provide a pre-operative "functional map" for neurosurgeons to improve surgical outcomes and decrease morbidity and mortality. Studies with MEG in childhood epilepsy have shown that it can accurately localize spike sources (both ictal and interictal) and characterize epileptiform disturbances. As an example, MEG may play a role in evaluating children with Landau-Keffler syndrome (LKS) and acquired epileptiform aphasia, both in diagnosis and in aiding presurgical localization of epileptiform activity when surgery is being considered; in addition MEG could help in identifying the generator of the paroxysmal partial discharges in Panayiotopoulos syndrome, or in scrutinizing the biomagnetoelectrical distinction between idiopathic and cryptogenic BECT.

It has been shown that MEG may play an important role in determining the significance of abnormalities seen on both structural and functional imaging, being used to identify spatiotemporal brain activation profiles associated with phonological decoding in dyslexic children and to study failure of left hemisphere posterior brain systems to function properly during reading in children with reading disabilities. Nonetheless, it has been used in recording evoked neural activity in children with autism, specific language impairment, Asperger syndrome or typical development.

These approaches may lead to a new way to study heart and brain functions and are utilized to expand detection and imaging technologies, to better investigate biological, physiological and pathological functions, and to develop clinical applications in normal children and in children with various disorders.

Jens Haueisen

Jens Haueisen received a M.S. and a Ph.D. in electrical engineering from the Technical University Ilmenau, Germany, in 1992 and 1996, respectively. From 1996 to 1998 he worked as a Post-Doc and from 1998 to 2005 as the head of the Biomagnetic Center, Friedrich-Schiller-University, Jena, Germany. Since 2005 he is Professor of Biomedical Engineering and directs the Institute of Biomedical Engineering and Informatics at the Technical University Ilmenau, Germany.
His research interests are in the numerical computation of bioelectric and biomagnetic fields and biological signal analysis

Biomagnetic measurement techniques

Jens Haueisen, Ph.D.

Institute of Biomedical Engineering and Informatics, Technical University of Ilmenau, and Biomagnetic Center, Department of Neurology, University of Jena, Germany

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Fetal magnetocardiography (fMCG) and fetal magnetoencephalography (fMEG) are recently established methods for the non-invasive assessment of fetal heart and brain function. The methods are based on measurements of the magnetic fields produced by the electric activities in the fetal heart and brain, respectively. The advantage of magnetic measurements is a significantly smaller amount of volume conductor influence as compared to electric measurements, which is especially important in the last trimester of gestation due to the electrically highly insulating vernix caseosa. One drawback is the very weak signal produced by the fetus, which makes very sensitive magnetic recording techniques and good shielding against external disturbances necessary.

In this review, the current state of the art in magnetic field recording techniques will be presented. Superconducting QUantum Interference Devices (SQUIDs) are the most sensitive commercial magnetic field or flux detector known today. Standard systems comprise about 50 to 300 SQUID sensors arranged in a fixed layout inside a cryostat and cooled by liquid helium. Alternative sensors operating at room temperature have been recently proposed. For example optical magnetic field sensors (optical pumping magnetometers) have the capability to record the fetal magnetocardiogram. The fact that optical magnetic field sensors do not need to be cryogenically cooled enables implementation of sensor modules that can be arranged in any geometrical configuration as required by the various clinical applications. An example for optimizing such configurations is given.

MCG lectures

Chair persons:
Peter van Leeuwen and Bettina F. Cuneo

Peter van Leeuwen

Peter van Leeuwen received a BEd in mathematics in 1971 from the Université de Montreal. After teaching, he switched to medical research in 1980 and obtained his PhD in medical science from the University of Witten/Herdecke, Germany in 1989. Here he also obtained his habilitation in electrophysiology in 2005. The main emphasis of his research work has been focused on non-invasive cardiology. Since 1992, he has been head of the Department of Biomagnetism of the Grönemeyer Institute of Microtherapy at the University of Witter/Herdecke, Germany. His research interests include biomagnetism, electrophysiology as well as nonlinear dynamics and he is presently pursuing projects in adult and fetal cardiology.

Processing and Analysis of fetal MCG data

Peter van Leeuwen

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When we place biomagnetic sensors near the abdomen of a pregnant woman, the signals we pick up contain information from various sources. Those that are of no interest to us are considered noise or confounding signals and those that we hope will give us answers to our questions are the signals of interest. Depending on what we are studying, the classification of the various signal components and the way we deal with them may differ.

This contribution will discuss such signals, how to identify them and separate from another and examine possible correlations between them. Apart from straightforward extraction of noise, methods for the identification and separation of the signal

contributions the mother and one or more fetuses will be presented. Furthermore, some approaches for the analysis of the different signal components will be described. These focus on the fetal components and include the determination of fetal heart rate and its variability, fetal cardiac conduction times, changes in signal morphology
associated with fetal movement or cardiac conduction disturbances. Furthermore, the influence of external factors on the fetal condition, such as maternal heart rate or respiration and uterine contractions will be considered. Applications of these analysis methods will be useful in both the study of normal physiological prenatal development and identification of pathological conditions in the fetus.

Uwe Schneider

Uwe Schneider, M.D., is Senior Registrar at the Department of Obstetrics of the Friedrich – Schiller University Hospital in Jena (FSU), Germany, where he also received his medical training. In 1996-1997 he has been working at the "Guy's and St. Thomas' Hospitals' Medical Schools (UMDS)", in London (UK). His research interest has always been focused on the evaluation of fetal Auditory Evoked cortical Fields performed by means of fetal Magnetoencephalography, as well as on the study of the development of the fetal autonomic nervous system and its possible disturbances by adverse intrauterine conditions by applying beat-to-beat fetal heart rate variability analysis from fetal magnetocardiographic recordings.

What does heart rate variability tell us about the development of autonomic nervous regulation during fetal life?

Schneider U.[1], Fiedler A.[1], Jaekel S.[1], Heinicke E.[1,2], Schleussner E.[1], Hoyer D.[2]

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We describe developmental aspects of sympatho-vagal heart rate regulation in human fetuses. In contrast to Doppler based cardiotocography, which the vast literature on autonomic development is based on, fetal heart-rate-variabilty (fHRV) derived from fetal

magnetocardiography (fMCG) enhances temporal acuity. We consider the gestational age (GA) and the fetal heart rate pattern (fHRP) representing the level of fetal activity (AL) as the major confounding factors in otherwise healthy and normal subjects.
We report on our data from normal fetuses in short and long (30 min) time series taken by a 31 channel gradiometer system or 155 vector magnetometer system, respectively, both comparable in terms of fHRV analysis. The AL were determined by visual blinded classification of the fetal heart rate patterns (fHRP); linear and non-linear fHRV parameters from the list of QRS time instants.
Assignment to AL plays a major role in the interpretation of fHRV since the distribution of the parameters and their interactions are strongly related to fHRP. Mean fHR is a cofactor related to that. We support the proposal of specific fetal frequency bands in fHRV, as suggested by David et al. 2007, and present the SDNN/RMSSD ratio as a measure of sympatho-vagal balance. Low activity fHRP (I) were characterized by significantly lower level fHRV indices and higher complexity when compared to fHRP II. We found that SDNN/RMSSD, LF/HF and mHR decrease with gestation in fHRP I, which suggests increasing vagal influence and that this decrease is more pronounced prior to 32 weeks GA. Beyond that GA SDNN/RMSSD is predominantly determined by RMSSD during fHRP I and by SDNN during fHRP II. In contrast to fHRP I, during fHRP II mHR is positively correlated to SDNN/RMSSD instead of SDNN > 32 wks GA. LF/HF increases in fHRP II during the first half of the third trimester. In fHRP III (assigned to active awake fetuses only after 32 weeks), highest level SDNN and mHR are associated with a dramatically reduced complexity.
Non-accelerative fHRP are indicative of parasympathetic dominance > 32 wks GA. In contrast, the sympathetic accentuation during accelerative fHRP is displayed in the interrelations between mHR, SDNN and SDNN/RMSSD. Prior 32 wks GA fHRV reveals the increasing activity of the respective branches of the autonomic nervous system differentiating the types of fHRP. The combination of high mHR, high SDNN/RMSSD and low complexity of the time series is referred to as the sympathetic triad.

Bettina Francesca Cuneo

During her fellowship, Dr. Cuneo's research project evaluating the effects of heart rate perturbation on cardiac output in the chick embryo won the Young Investigator Award at the American Academy of Pediatrics in 1989. Following her fellowship Dr Cuneo became the first full time cardiologist in the Chicago area specializing in diagnosis and care of the fetus with heart disease. She has collaborated with Ronald Wakai, Ph.D and Janette Strasburger M.D. and together they have developed and advanced the field of "fetal electrophysiology". Using the technique of magnetocardiography, the findings by this team have provided unique insight into the clinical care and understanding of fetal cardiac electrophysiology and arrhythmias, and have improved the outcome of high risk pregnancies. Currently, Dr. Cuneo is Associate Professor of Pediatrics and Obstetrics at Rush Medical College and Director of Perinatal Cardiology at The Heart Institute for Children & Advocate Health Care.

Clinical Usefulness of Fetal MCG in the Diagnosis and Management of the Fetus with, and at risk for, Arrhythmia

Bettina Francesca Cuneo, M.D.

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Background: Fetal arrhythmias constitute 10-20% of referrals to the perinatal cardiologist. In addition, there is a substantial population of fetuses at risk for developing arrhythmias due to associated congenital heart disease, or because of a family history of genetic arrhythmia or maternal Sjogren's antibodies. Both acute and prospective evaluation of the fetus is performed by Doppler and M-Mode echocardiography, which, because it assess only the mechanical consequences of electrophysiological events, provides an incomplete picture of the fetal electrophysiological state. Obviously, fetal magnetocardiography (fMCG) or electrocardiography (fECG) refines and uncovers

subtleties the diagnosis of arrhythmia and the prospective evaluation of the at-risk fetus, but it has not been evaluated if and how fMCG impacts the clinical management of the fetus with or at risk for, arrhythmia. The purpose of this study was to review our experience with fMCG in the clinical diagnosis and management of the pregnancy complicated by or at risk for fetal arrhythmia.

Methods: We reviewed the magnetocardiograms and medical records of fetuses referred to the Biomagnetism Laboratory at the University of Wisconsin Madison with either a history of intermittent and sustained arrhythmia or risk factors for arrhythmia, including a family history of genetic arrhythmia, concomitant congenital heart disease, previous unexplained fetal demise or maternal sjogren's antibodies. Fetuses were studied in the baseline state, and whenever possible, after pharmacologic or catheter interventional. We evaluated the accuracy of echo compared to fMCG by comparing the echo diagnosis made by the referring physician with the fMCG findings, and assessed the impact on clinical management of the pregnancy.

Results: Over a 9 year period, 214 fetuses with arrhythmia or at risk for arrhythmia were evaluated by 1-3 (mean 2) fMCG as summarized in ***Table 1***:

Indication for fMCG	N		Indication for fMCG	N
Arrhythmia	**146**		**At risk for arrhythmia**	**68**
Irregular Rhythm	**25**		Rhabdomyoma	7
Bradycardia	**61**		Ebsteins/TVD	5
AV block	45		Aortic Stenosis	5
Blocked PAC	8		Cardiomyopathy	5
Sinus	8		SSA/SSB antibodies	25
Tachycardia	**60**		FH Arrhythmia	10
SVT	38		Previous IUFD	11
Sinus	7			
A flutter	15			
V tach	5			

Of those fetuses with arrhythmia, a post-fMCG diagnosis was confirmatory in 60% and different enough from the pre-fMCG diagnosis to alter clinical management in 40%. Six fetuses thought to have AV block prior to fMCG had blocked atrial bigeminy. 2°AV block was diagnosed by echocardiography in ° in 3 fetuses while fMCG demonstrated 3° AV block with isorhythmic AV dissociation.

All mothers of fetuses presenting with risk factors for arrhythmia could reassured that cardiac intervals were normal, including 2 with prolonged mechanical PR intervals that showed intraatrial conduction delay by fMCG.

Of fetuses with aortic stenosis, the findings of repolarization abnormalities improving after in utero balloon dilatation supported that intervention in 2/4 fetuses. The rhythm during decelerations in 3 of 4 fetuses with tricuspid valve disease was diagnosed by fMCG to be transient 2° AV block rather than sinus bradycardia. Two fetuses died within 2 weeks of the fMCG, which promited the earlier delivery of subsequent live-born infants.

Conclusions: fMCG had a profound impact both on the clinical management of the fetus with arrhythmia and the fetus at risk for arrhythmia. Not only is the diagnosis accurate and more complete when compared to echocardiography alone, but supportive evidence for fetal intervention or timely delivery can be identified. Further prospective evaluation may identify electrophysiological findings that support in utero treatment with specific antiarrhythmic medications or identify proarrhythmia when such medications are given.

Janette F. Strasburger

Janette Strasburger, MD is Director of Cardiac Services for Children's Hospital of Wisconsin – Fox Valley, and a Professor of Pediatrics at the Medical College of Wisconsin. She is a graduate of the University of Nebraska School of Medicine, completed her Pediatric Cardiology and Electrophysiology Fellowships at Baylor College of Medicine, Houston Texas, and served on the faculty of Northwestern University and Children's Memorial Hospital in Chicago, Il. In January 2002, she accepted her present appointment at the Children's Hospital of Wisconsin. Her research interests are in combined imaging modalities for fetal diagnosis, as well as in fetal electrophysiology. She has collaborated with Ronald T. Wakai, PhD on fetal magnetocardiography projects for over 8 years, and she is currently evaluating simultaneous Doppler echocardiography and fMCG for beat-to-beat electromechanical characteristics of the human fetal heart.

Simultaneous Fetal Magnetocardiography and Echocardiography

Janette F. Strasburger, M.D.

Children's Hospital of Wisconsin, Fox Valley and Medical College of Wisconsin (Wisconsin – USA)

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Background: The ability to combine two diagnostic imaging modalities provides unique data that neither procedure alone could provide. We hypothesized that simultaneous fetal

magnetocardiography (fMCG) and echocardiography/Doppler (echo/Doppler) would enhance diagnostic assessment of the human fetus during arrhythmias.

Methods: 113 studies in 84 subjects have been performed simultaneously without complication to the research subject. Participants ranged from 19-35 weeks gestation, and included 15 normal volunteers, 10 with abnormal fetal diagnosis but normal fmcg , 16 with fetal ectopy, 5 supraventricular tachycardia, 1 atrial flutter, 1 ventricular tachycardia, 4 genetic ion channelopathies, 4 SSA/SSB positive without heart block, and 18 with 2nd or 3rd degree AV block. 9 of these patients had structural heart disease and one had myocarditis. One or more 10 minute fMCG runs were initially performed to establish underlying fMCG findings. Then 1 to 4 five-minute runs were recorded, prolonging the evaluation of the subject by about 30 minutes. Doppler recordings were obtained from various standard sites within the fetal heart using either a curvilinear transducer or an adult cardiac transducer, with a battery-operated Sonosite Titan II ultrasound device. Tracings were combined by means of a periodic marker channel in both recordings. Combined tracings were accurate to within +/- 2 ms (1 pixal). The device was turned off during the last 30 seconds of the recording to provide a noise-free template for alignment and identification of the various fMCG signal components. Post-processing for extraction of noise was performed prior to alignment. Alignment of Doppler and fMCG signals was achieved by using continuous Sony digital recording of echo/Doppler utilizing Matlab software. 85% of all tracings were alienable.

Results: In normal subjects, the pre-ejection period of the fetal heart (time from onset of QRS complex to onset of aortic outflow) ranged from 40-80 ms. Prolonged pre-ejection periods were seen in severe fetal disease states. Marked variability in pre-ejection periods and ejection times (onset to end of Doppler aortic duration) were also seen in both tachy and bradyarrhythmias. Doppler of atrial events helped identify AV dissociation in early gestation fetuses. Validation of P wave morphology and mechanical PR interval was possible in about 10% of fetal tracings.

Conclusions: Simultaneous fMCG/Doppler provided useful supplementary diagnostic information and enhanced assessment of the fetus. Additional study of its role in arrhythmia diagnosis and management is required as well as development of bioinstrumentation capable of performing and automating these new measurements

MEG lectures

Chair persons:
Yoshio Okada and Uwe Schneider

Hubert Preissl

Hubert Preissl received the diploma in physics and the Ph.D. degree in physics, both from the University of Tübingen, Tübingen, Germany, in 1988 and 1994, respectively. He was with the Max Planck Institute for Biological Cybernetics, Tübingen, until 1994. He then joined the Institute for Medical Psychology and Behavioral Neuroscience, University of Tübingen. In 1997, he became an Assistant Professor with the MEG Center, Tübingen. In addition, since 2000, he has been a Project Director with the Fetal Magnetoencephalography Laboratory, Little Rock, AR.

Fetal Magnetoencephalography: Extraction of fetal brain signals in the presences of large interfering signal sources

Hubert Preissl

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The assessment of the neurological integrity of the human fetus in utero is a technically challenging problem. New brain imaging devices, like fetal magnetoencephalography, can substantially improve our capabilities to describe functional brain activity in the fetus. However the fetal brain signals are low amplitude signals and recorded in the presence of large interfering sources. For the analysis several different approaches can be used and one has to be aware of its possible problems.

It has been well established by fetal behavioral studies and investigations in preterm and term newborns that the brain is functional in utero. The major effort required to perform effective neurological functional investigations is designation of an integrated approach to neurological assessment and the generation of normative data. Currently, it is possible to record evoked brain activity elicited by auditory and visual stimulation from the fetus. In addition, there is growing evidence that spontaneous brain activity can be recorded in the fetus. In my talk, I will show the current status of the brain imaging field for fetal investigations.

Ronald T. Wakai

Ronald Wakai is Professor of Medical Physics at the University of Wisconsin-Madison. He received a bachelor's degree in Physics in 1980 from Cornell University in Ithaca, New York and a Ph.D. in Physics in 1987 from the University of Illinois in Urbana, Illinois. His thesis research was on the signal and noise properties of microfabricated dc SQUIDs, performed under the direction of Professor Dale Van Harlingen. In 1987 he moved to the University of Wisconsin-Madison, where he became a postdoctoral scientist in the Medical Physics department, working under Professor John Cameron. He joined the faculty the following year. His group was one of the first to apply MCG and MEG to the fetus and neonate, and he has devoted most of his career to research in these areas. He has held a joint appointment with the Neurology Department at UW-Madison and Visiting Professor appointments with the University of Sao Paulo-Ribeirao Preto.

Perinatal MEG

Ronald T. Wakai, Ph.D.

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The perinatal period is a fascinating time to study electrical brain activity. The developmental changes are so rapid that they can be seen from week to week. Although EEG provides an extremely sensitive indicator of developmental changes, it suffers from a lack of specificity. In the last years, MEG has begun to attract considerable attention for fetal and neonatal applications. Fetal MEG is capable of directly recording human brain activity in utero, while neonatal MEG provides a combination of spatial and temporal resolution unavailable with other techniques. This talk presents some of the opportunities and challenges facing the nascent field of perinatal MEG.

Elina Pihko

Elina Pihko (former Kaukoranta), Ph.D., Docent. She did her PhD (1986) in the Low Temperature Laboratory of Helsinki University of Technology. After these early neuromagnetic studies on somatosensory and pain processing, she studied auditory change detection first with MEG and then with EEG in the University of Jyväskylä (1992-2000), where she got involved in infant studies. In 2000 she joined the BioMag Laboratory in the Helsinki University Central Hospital, where she continued paediatric studies with MEG. Parallel with studies on normal development of auditory language system and somatosensory cortical areas in babies and children, her group has studied, e.g., the effect of rehabilitation on brain responses in children with language and somatomotor problems. Recent focus has been on studies of newborns at risk for neurological sequelae due to preterm birth or fetal exposure to opioids. Currently she is working in the Low Temperature Laboratory.

MEG in neonatology: Somatosensory cortical processing in healthy and at-risk babies

Elina Pihko, Ph.D.

Helsinki University of Technology

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Magnetoencephalography (MEG) is a promising research tool for Perinatal examinations. MEG is totally noninvasive, silent and has millisecond-range time sensitivity, as does EEG. However, unlike EEG the MEG signal is relatively insensitive to variations in skull thickness and conductivity and is thus less distorted by open fontanels and sutures of the infant skull. Thus, accurate determination of active cortical areas in infants is possible

using MEG. We used MEG to study cortical processing of somatosensory information in healthy neonates and infants. Touch activates primary and secondary somatosensory cortices, but the timing and other details of cortical activation differ from those of mature responses. In neonates, tactile stimulation of an index finger activates contralateral primary somatosensory cortex with a peak latency of 60 ms (M60 response) and ipsi and contralateral secondary somatosensory cortices at about 200 ms (M200) [Nevalainen et al., NeuroImage 40 (2008) 738–745]. The responses gradually mature, and at the age of 2 years the cortical sources underlying the responses resemble those of adults.

Since prematurely born infants are at risk for impairments of the sensorimotor development, we recorded somatosensory evoked magnetic fields in very prematurely born infants at term age and in healthy neonates born at full term in order to determine possible differences in the function of somatosensory cortices. The following are preliminary results of a large ongoing study of very prematurely born infants. Similar response latencies of M60 and M200 in the two groups indicate normally developed conduction in somatosensory system of the prematurely born infants. However, the strength of the M60 response from the primary Somatosensory cortex was significantly lower in the premature infants at the group level. This may reflect weaker synchrony in firing or a smaller number of cortical neurons activated by the somatosensory stimulation. We further discovered a lack of M200 response in 4 preterm infants all of whom had an anatomical lesion in the same hemisphere where the M200 response was missing [Nevalainen et al., Int J Psychophysiol 68 (2008) 85–93]. Further analyses of the MEG results in connection with clinical data will be performed after completion of the follow-up study.

We have demonstrated that MEG is a useful clinical tool to study the development of the somatosensory system. Very prematurely born infants can be safely and noninvasively studied at term age, at which time it is possible to demonstrate some defects in somatosensory processing.

Yoshio Okada

Yoshio Okada, PhD, Professor of Neurology and Neurosciences, Director of Biomedical Research and Integrative Neuro-(BRaIN) Imaging Center, University of New Mexico Health Science Center, Albuquerque, NM 87131 USA. Dr. Okada received his PhD in 1980 in mathematical psychology from Rockefeller University. He then began his work in MEG and EEG as a postdoctoral scientist at New York University under Samuel Williamson and Lloyd Kaufman. In 1984 he started Magnetophysiology Laboratory at the NYU Medical Center in Dept. Physiology and Biophysics. In 1989 he moved to University of New Mexico as Co-Director of the Center for MEG. In 2001 he started the Center of Biomedical Research Excellence at the UNM Health Science Center. In 2005 he constructed BRaIN Imaging Center in a 1000-m2 state-of-the-art multimodal neuroimaging facility that includes 4.7T MRI, EPR 3D imager, 2-photon optical, patch-clamp electrophysiology, EEG, MEG and cellular/molecular biology. Dr. Okada is an inventor of a neonatal mobile MEG system called babySQUID.

Neonatal brain development in patients with brain disorders.

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We have used a neonatal MEG system designed specifically for assessment of brain functions in newborns, infants and young children, to look for abnormalities in the brain of children with cerebral palsy (CP), epilepsy and autism spectrum disorder (ASD). In children with CP, there was evidence for intra- (abnormal somatotopic projections in the "affected" hemisphere) and interhemispheric reorganization (abnormal somatotopic projections in the "unaffected" hemisphere). In children with neocortical epilepsy, there

was a high-frequency signal (70-120 Hz) superimposed on a subset, but not in all the interictal spikes. This may be analogous to the so-called “fast ripple” in the adult epilepsy literature and might be a biomarker of epileptogenic regions in the cortex. In children with ASD, there was evidence for delayed communication between the somatosensory and auditory cortices in 3-year old children with ASD compared to typically developing controls, suggesting that their long-range cortico-cortical communication may be slower.

Round Table

Biomagnetism in Perinatal Medicine: how can new technologies help sick fetus/infant?

Chair persons:

Silvia Comani and Janette Strasburger

Mario Fulcheri

Mario Fulcheri is M.D., psychiatrist, psychotherapist, Full Professor in Clinical Psychology and President of the Master's Degree Course in "Clinical and Health Psychology" at the University "G. D'Annunzio" of Chieti-Pescara (Italy). He is partner, founder and delegate adviser of the Counseling for the "University Association for the Development and Formation to the Relationship of Help and Counseling" (AURAC), founded in January 2002. He is fellow of the ICPM (International College of Psychosomatic Medicine) and member of the Italian Psychosomatic Medicine Society (SIMP). He is author of more than 250 publications on international journals and books on psychiatry, psychotherapy and clinical psychology.

Remarks on current Perinatal Clinical Psychology

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Perinatal Clinical Psychology is a psychological discipline born from the interaction between medical, psychological, pedagogical, humanistic and social scientific knowledge.

The objects of study of this discipline are the following: the development of mental structures in fetus and infant; the relations between pregnant woman-fetus, mother-infant and parents-infant; the modifications of the mother's mind; the ways of assistance in relation to pregnancy and childbirth.

Pregnancy represents a period of profound transformations, both physical and mental; it is also characterized to the presence of symptomathologies and pathologies, such as hypersomnia, first quarter hyperemesis, pseudocyesis, miscarriage and gestos. Moreover, there are some psychopathological conditions following the childbirth, such as post-partum blues, post-partum depression and post-partum psychosis. There are a number of

studies attempting the investigation of the influence of birth's outcome variables, such as the type of delivery, the quality of the relationship with the accompaniment to birth figures, anxiety, stress and pain.
Recent contributions coming from Positive Psychology that attempt to analyze the relation between parenthood and quality of experience in daily life. Indeed, parenthood implies a radical overhaul of individuals' hierarchy of values; it requires an experiential adjustment to new environmental challenges, and a redistribution of the psychic resources. Therefore parenthood is an emergent source of opportunities for action and for individual development (requires the acquisition of new skills, at the individual as well as at the interpersonal level), promoting and enhancing complexity in behavior.

Contributed papers

ID 421001

Fetal Heart Rate Patterns Develop Like a Self-Organization Process

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Background: The evaluation of key parameters of fetal development with respect to an appropriate systems theoretical concept namely self-organization could essentially foster the early detection of developmental problems and hence the design of therapeutic strategies. From that point of view self-organization may be defined as: (i) Evolution of a previously less organized system into a higher organized one in the absence of external control. (ii) Movement from a large region of state space to a persistent smaller one, under the control of the system itself. (iii) Development of correlations over time or space of previously independent variables operating under local rules. Fetal heart rate patterns reflect respective aspects of cardiovascular autonomic control.
Aim: The present work aims to explore whether heart rate patterns during the fetal development show characteristics of self-organization.
Study design: From 78 normal fetuses, gestational age 23-40 weeks, heart beat interval series of 30 min duration were recorded by magnetocardiography with a sampling rate of 1 kHz. Several indices which are typically associated with self-organization were analysed and related to fetal development.
Results: With development (a) the variability of heart rate increased, (b) the number of acceleration increased, (c) autonomic information flow increased over large time scales. These features are associated with essential self-organization characteristics, namely necessary variability (a), loss of degrees of freedom (b), and emergence of global order (c).
Conclusion: Heart rate characteristics interpreted following the systems theoretic concept of self-organization may provide new insights into the fetal development with implications for more appropriate diagnosis and elaborated treatment of adverse prenatal environmental influences.

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ID 421002

Use of spatiotemporal signal space separation for head coordinate transformation in children

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Introduction: Spatiotemporal signal space separation (SSS) was designed to reduce artifacts from external magnetic source by Taulu et al [1]. Recently, investigators have used the spatiotemporal SSS to achieve movement correction in children having epilepsy [2]. We have used this technique to achieve head coordinate transformation in children during cognitive experiments.

Methods: Data was collected from seven children (mean age: 8 years 5 months). Children performed a cued Go/NoGo auditory task. Brain signals were recorded using 306 channel whole head MEG system (VectorView, Elekta Neuromag, Helsinki, Finland). Individual head positions were transformed into a common position using MaxFilter (Elekta Neuromag, Helsinki, Finland).

Results: Head coordinate was successfully registered to the device center coordinate after spatiotemporal SSS in 7 children during Go/NoGo task. We achieved individual as well as group head position compensation (Fig. 1). Before spatiotemporal SSS filtering (left side of Fig. 1) it is difficult to define peak latency. However, after filtering (right side of Fig. 1), the wave is clear enough to define peak latency.

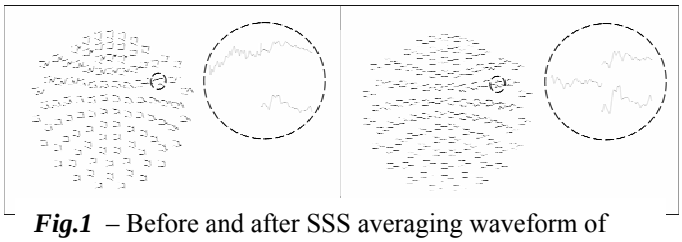

Fig.1 – Before and after SSS averaging waveform of E.K. during Go condition

Discussion: In conclusion, spatiotemporal SSS is a strong tool in analysis of MEG in children during cognitive study. In future fetal MEG reserch, we suggest that SSS could help transform individual fetal data to device center coordinate.

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ID 421003

Pre-ejection Periods Associated with Different Cardiac Disease States in the Human Fetus

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Pre-ejection period (PEP) is the combined measure of electromechanical delay and isovolumetric contraction of the cardiac ventricles. Important electrophysiological intervals and ventricular function associated with cardiac compromise, arrhythmias or structural heart disease can be measured using simultaneous fMCG and Doppler Ultrasound, which assess the magneto-mechanical function of the fetal heart. PEP measured in normal control fetal groups differ significantly from groups in which cardiac compromise, arrhythmias and structural heart disease exist. Our study sheds light on these differences.

Moving the fetal MCG out of the shielded room into the clinic

ten Haken B.[1], Krooshoop H.J.G.[1], van Gendt M.J.[1], Dielhoff T.[1], Quartero H.W.P. [2], ter Brake H.J.M.[1]

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The FHARMON (Fetal HeArtMONitor) project aims at developing a closed helium cooling system which is easy to use in clinical environments with its 'plug and play' capability. The cryogenics cool two 2nd order gradiometers and eight reference sensors in a low T_c SQUID system which can measure an fMCG with a sensitivity up to 10fT $Hz^{-1/2}$ [1]. Previously, fMCG measurements were done inside the magnetically shielded room (MSR). To demonstrate the systems clinical usability, the fMCG is measured outside the MSR. By measuring outside the MSR new magnetic noise sources arise, such as 50-60Hz power lines, elevators, RF-noise and the earth magnetic field. These interferences can be suppressed by local shielding or the use of an optimized 3rd order gradiometer [2]. Sources close to the fetal heart have larger gradients than sources from further away and are therefore more difficult to filter using gradiometers. A commonly neglected interfering source close to the fetal heart is the maternal liver, which in some anomalies can hold an amount of 10 times the normal level of iron. The respiratory movement causes the liver to move in the earth magnetic field, which was suppressed about a factor 1000 in the MSR, and become magnetized. With a magnetic susceptibility of $\chi_v = 8.4 \times 10^{-6}$ a healthy liver acts as a magnetic dipole of ($\sim 1.2 \times 10^{-6}$ Am^2). Preliminary approximations show a field of 20pT at 0.10m distance from the liver, this in contrast with the fetal heart signal which hardly exceeds 10pT. In the continuation of the project new experiments show how the liver influences the measurements and how adaptive combination of the 2nd order gradiometers will improve suppression of additional noise in the unshielded environment.

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ID 421005

Metrological aspects of a fetal magnetocardiography

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The paper presents a study to establish the metrological aspects for a fetal magnetocardiography. The measurements must be made in a shielded room, in order to avoid an abundance of environmental noise. The shielded room is placed in the center of a triaxial Helmholtz coil system of big dimensions for dynamic control and compensation of the natural geomagnetic perturbations. The shielding is carried out in two ways. The shielded room accomplishes the shielding of medium and high frequency electromagnetic fields. For geomagnetic and very low frequencies field, the dynamic compensation method is used, which ensures the field control down to near zero values. To detect the fMCG signal is used a SQUID device with three orthogonal channels. Because the fMCG signal is very low (about 100 fT), the automatic control system must assure a residual noise level of the field much lower than the fMCG. For metrological calibration of the installation, on propose the using of a fetal magnetocardiographyc signal simulator. This simulator consists in a triaxial Helmholtz coil system through which is passed a current to generate a magnetic field with the intensity equal with the fetal magnetocardigraphyc signal.
We propose a detection method of the fetal magnetocardiographyc signal by using a grid with 3*3 measurement points with the center in the umbilical area. Starting clockwise from the center the sensor is moved from point to point until the fetal magnetocardiographyc signal is detected.

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ID 421006

Spectral analysis in the detection of fetal respiratory sinus arrhythmia

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The initiation of fetal breathing movements in the second trimester of pregnancy is a sign of maturation and development. Fetal magnetocardiography permits the determination of high resolution fetal heart period time series. We have developed a procedure which exploits the effect of respiratory sinus arrhythmia (RSA) on such time series and permits the identification of periods of breathing movements. Magnetocardiograms were recorded in fetuses in the second and third trimester of pregnancy. Signal processing using templates and correlation analysis were applied in order to identify fetal R peaks (1 ms precision) and the corresponding RR interval time series were constructed. A program was developed which reads in fetal RR time series and displays them in both the time and frequency domain. The plot of the RR interval time series over time permits the visual identification of possible fetal RSA. The display of the frequency spectrum of the complete time series between 0-2 Hz indicates whether dominant, persistent breathing movements are present. As the episodes of breathing movements may be only a few seconds short, the frequency spectrum can be calculated for subseries within user-specified time windows. The spectra of the subseries can be viewed singly (2-D) and as a function of time (3-D). Fetal breathing movements may be presumed when the subseries spectra consistently demonstrate a peak at a specific frequency between 0.4 and 1.4 Hz over episodes with a duration > 5 s. We present a number of fetal RR interval time series acquired from different gestational ages in which episodes of fetal breathing movements can be identified persisting for various durations at different frequencies. Comparing these with data without such spectral characteristics indicate that this data analysis approach is suited for the identification of fetal breathing movements by examining the frequency spectra of the heart period time series.

ID 421007

Somatosensory Evoked Magnetic Fields in Very Low Birth Weight Infants

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Introduction: Increased survival of very low birth weight (VLBW) infants is one of the major achievements in contemporary neonatal medicine. Improving neurological outcome of these infants still requires finding of new prognostic methods and further understanding of the underlying mechanisms of the most commonly seen disabilities. We aimed at determining possible differences in early somatosensory processing between the VLBW infants and controls.

Methods: We performed MEG recordings for 16 VLBW infants and 16 healthy term newborns. Somatosensory evoked magnetic fields (SEFs) were recorded from the contralateral hemisphere to stimulation of the left index finger during natural sleep. The infants form a part of a larger multimethodological study still in progress.

Results: In both groups, two major SEF components were identified with approximate latencies of 60 (M60) and 200 ms (M200). The major difference between the groups was the significantly weaker source strength of the M60 in the patients than controls ($p<0.05$). In four VLBW infants the later M200 response was absent or could not be modeled. Cranial ultrasound and/or magnetic resonance imaging revealed lesions of the underlying hemisphere in all these four infants.

Discussion: The differences in the SEFs between the patients and controls indicate that preterm birth and associated conditions may alter the functioning of the somatosensory cortex. The lower ECD strength of M60 may reflect weaker synchrony in firing or a smaller number of simultaneously activated cortical neurons. At the individual level, the lack of the M200 coexisted with abnormal anatomical findings in four VLBW infants. The prognostic significance remains a subject for our ongoing follow-up study.

ID 421008

Neonatal Auditory and Somatosensory Evoked Magnetic Fields

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Magnetoencephalography provides noninvasive means for studying brain functions in neonates. Somatosensory and auditory evoked magnetic fields have successfully been measured in newborn babies. Somatosensory evoked fields have shown that, in neonates, both primary and secondary somatosensory cortices are activated by tactile stimulation [1]. Auditory evoked fields have been measured to study sound discrimination abilities in young infants. However, the locations of the generators of the auditory evoked fields have only rarely been assessed [2,3,4]. We recorded, in the same experiment, both auditory and somatosensory evoked fields from the same neonates in order to compare the locations of the underlying sources. The subjects were 10 healthy full term newborns. Tactile stimulus was given to the right index finger every 2 seconds. Alternately, every 2 seconds, a sound (vowel 'a') was delivered monaurally to the right ear of the subject. Evoked fields were recorded (Elekta Neuromag Oy, Finland) from the contralateral hemisphere. We calculated equivalent current dipoles (ECDs) for the two main somatosensory responses (M60 and M200) and for the main auditory response (M300). The coordinates of the ECDs differed between the current sources: M60 was located more superior than M200 and M300, whereas M300 was located more lateral than M60 and M200. The locations are consistent with M60 and M200 originating in the primary and secondary somatosensory cortices, respectively, and the location of M300 agrees with a source in the auditory cortex.

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ID 421009

Doppler extended-Flow and fetal echocardiography during routine first-trimester screening in unselected population

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Introduction: Prenatal diagnosis of structural heart defects has been shown to have a major impact on the prenatal and postnatal management of affected pregnancies. Fetal echocardiography is usually performed in the midtrimester. However, with modern ultrasound equipment, one can examine fetal heart structure and function much earlier in pregnancy. The increasing practice of early fetal echocardiography has been mainly targeted at selected high-risk populations, and only few studies report on low-risk populations in early second trimester. Modern ultrasound equipment and new technologies applied to prenatal diagnosis allow detection of fetal anomalies, particularly heart anomalies. This study was conducted to explore the percentage of cases in which an adequate complete examination of the fetal heart was possible at a gestation less than 15 weeks using extended flow technology.

Methods: This was a cross-sectional study of 73 fetuses in unselected singleton pregnancies during routine ultrasound screening at the Prenatal Diagnosis Unit, University of Chieti. The fetuses underwent detailed fetal echocardiography at a gestational age below 15 completed weeks during routine genetic sonogram by a single experienced operator. Maternal body mass index, placental site, fetal position, time-spending during fetal heart evaluation and fetal heart structures were recorded for each exam. Situs, 4-chamber view, septum primum, foramina ovale, ventricular septum, atrio-ventricular valves, aortic and pulmonic valves, three vessel view, V-sign, vene cavae, pulmonary veins view were recorded, if correctly identified during the examination. All pregnancies underwent routine morphology scan at 20 and 28 weeks' gestation. After birth, all neonates underwent clinical examination by experienced neonatologists.

Results: 68 exams out of 73 were performed within 5 minutes during genetic sonogram. 68 exams completed the checklist for cardiac morphology. The four examinations uncompleted were due to miss depiction of V sign and pulmonary veins in two fetuses, and pulmonary veins in the last two, although normal maternal BMI and different fetal position.

Discussion: The mainstay of the present study is that, by using modern technologies in prenatal ultrasound such as extended flow, fetal cardiac morphology can be explored completely as routine examination within genetic sonogram in low risk patients. Experienced operators are needed for correct analysis of genetic sonogram and further formation in fetal cardiology using extended flow is easily reached. Extended flow technology seems to be helpful in completing cardiac morphology much earlier than routine scan. Overlooking during late first and early second trimester of pregnancy could be useless, particularly if exposure time is longer than normal, which could not be the case. If higher output levels are needed to obtain diagnostic information, exposure time should be reduced accordingly.

ID 421010

Perinatal Psychosomatic Research

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The present work moves its argument from the assumption that pregnancy represents a period of profound and highly psychosomatic transformations. In our contribution will be described the symptomathologies and pathologies verifiable during pregnancy, such as hypersomnia, first quarter hyperemesis, pseudocyesis, miscarriage and gestos. Further on, the topics of birth – and pain and fear associated with it – and the relation mother-father-child at the moment of childbirth will be analyzed.

Recent contributions coming from "Infant Research" assume that the function of the first relationship between mother and child is the key element in the transition from body to mind, therefore the matrix of the psychic development of the child. To this regard, Imbasciati (2006) proposed the "Theory of the Protomental": it explores the transition from the non-mental – attributable to somatic and then neurologic components – to primary psychological processes, and thus to the birth of the mind.

Nowdays perinatal research in psychosomatics is rich but nonhomogeneous. Indeed several studies focus on the following topics: the endocrinous facet – putting aside or subtending the psychic one without any development; psychological symptoms; the mother's psyche and her personality structure.

Finally, will be presented a number of studies attempting the investigation of the influence of birth's outcome variables, such as the type of delivery, the quality of the relationship with the accompaniment to birth figures, anxiety, stress and pain.

ID 421011

Clinical Psychology In Perinatal Context

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Over the last twenty years, two fundamental conditions led to the birth and development of a specific area of Applied Clinical Psychology definable as Perinatal Clinical Psychology: research on intrauterine life (gestation and childbirth) and on the quality of the primary relation to one hand, the influence of communication and social-cultural impulses on parenting (both maternal and paternal), together with several welfare components to the other.

Perinatal Clinical Psychology is a psychological discipline grounded and born from the interaction between medical knowledge and psychological, pedagogical, humanistic and social scientific ones.

The objects of study of this discipline are the following: the development of mental structures in fetus and infant; the relations between pregnant woman-fetus and mother-infant; the modifications of the mother's mind; the ways of assistance in relation to pregnancy and childbirth.

Our aim is to explore the prenatal development from a multidisciplinary and holistic point of view, including biological, psychological and anthropological perspectives and contributions. The main topics of the present work are: the role of Cliinical Psychology applied to prenatal events; the research clinical consult as a useful tool to analyze psychological experiences and dynamics characterizing the phase of pregnancy; the antenatal prevention in relation to psychoprophylaxis; prenatal education and accompaniment during pregnancy and preparation to birth.

ID 421012

Characterization of Mu-rhythm in Children Aged 3-9 Month-old.

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Mu-rhythm (μ) is an idling rhythm that originates from somatomotor cortex during rest. The frequency of μ gradually increases to the adult value (~10 Hz), although limited results are available from children [1]. It has also been proposed that modulations in μ reflect activation of the Mirror Neuron System (MNS), since it desynchronizes in response to execution and observation of movements [2]. The aim of this study was to measure Rolandic μ during rest and movement in a sample of 3-9 month old infants using a pediatric MEG system (babySQUID)[3]. Ten 3-9 month old typically developing infants participated in the experiment. BabySQUID measurements were performed over the left hemisphere for two 5-minute sessions. Each subject participated in two intermixed conditions, the Control condition and the Movement condition. The former was used to detect the baseline or idling μ. In the Movement condition the infant squeezed a pipette with the right hand. This pipette was connected to a pressure transducer to record the movement. The pressure waveform was synchronized with the MEG data. The power spectrum of MEG data was obtained to identify μ activity. In the fronto-parietal area of the infants' brain, μ was found across all participants during the Control condition. The μ peak frequency in the 3-month old group (N=4) ranges between 2.5 and 3.5 Hz, and is 3.5 and 4 Hz respectively in the two 6-month old subjects. To the best of our knowledge, this is the first evidence of μ in infants under 6 months of age [4]. A gradual shift towards higher frequencies, included between 4.8 and 5.3 Hz, is observed for the 9-month old group (N=4). The current results may contribute to a better understanding of MNS developmental trajectories and to the development of diagnostic and therapeutic tools.

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ID 421013

Increases in Coherence Index with Age in Neurotypical Children

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Coherence has long been used to study connectivity between different brain areas primarily in EEG. While this approach has received criticism over the years, if the analysis approach is properly implemented and the constraints of the method accounted for when interpreting the results, it still remains one of the most powerful ways to study cortical connectivity using MEG/EEG. The aim of the study was to examine the index of cortico-cortical connectivity in the developing brain. Based on the rapid development of the brain across the age range studied including increased myelination and synaptic connections, we hypothesized that the strength of the cortical connectivity would increase with age. The MEG data were collected using the prototype pediatric MEG system called babySQUID [1] from 13 children ranging in age from 6-48 months (mean age = 33.31 months ± 5.62). As part of a larger study we collected two minutes of spontaneous brain activity at the beginning of each data collection. This spontaneous activity was analyzed for cortical connectivity during sleep using standard coherence analysis (1-15 Hz) comparing coherence between each channel pair. This information was reduced to a coherence index by normalizing the coherence by the distance between channels and the number of channels. We have obtained novel results regarding an increase in coherence index with age (correlation between coherence index by age comparison $r = 0.62$, $p < 0.02$ – see Fig. 1). The results are consistent with our hypothesis that cortical connectivity will improve with age. This extends previous EEG results showing a general increase in coherence with age in older children [2].

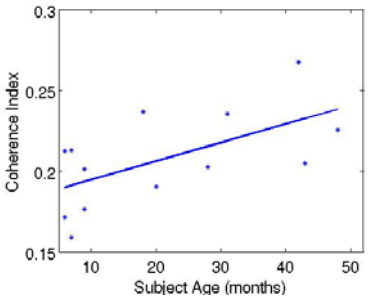

Fig. 1. Coherence index by age neurotypical children.

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ID 421014

ICA Segmentation Method to Separate the Fetal Magnetocardiogram from fMCG Signals Affected by Fetal Movements

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Independent component analysis (ICA) is largely applied to fetal magnetocardiography (fMCG) to estimate the source signal of fetal heart activity. Fetal movements during fMCG have an important effect on the fetal cardiac signal detection because they imply a change in the position and orientation of the fetal heart and can affect the features of the magnetic source signals while they are recorded, with consequent potential detriment of ICA performance in reconstructing the fetal cardiac signal. This work proposes a segmented ICA method to reduce the effect of fetal movements on ICA performance. When fetal motion is present in the fetal signals separated with ICA, the movement transients are automatically selected by negentropy criteria. The fMCG original data are then segmented in distinct motionless intervals using negentropy transients. The complete signal must be divided in as many segments as required by the number of detected motion transients. Then, source separation with ICA is performed again for each time segment separately using the desired parametric choices. We applied this method to 13 fMCG data sets (recorded with a 55–channel low-temperature dc-SQUID system - ATB Argos 200) affected by fetal movements. The fetal and maternal heart activity were estimated using the fixed-point ICA algorithm (FastICA) [1,2,3]. When fMCG data are segmented in motionless segments, ICA source separation is more effective, resulting in recovered fetal traces with better waveform. Our preliminary results show that, in cases when significant fetal motion is present, ICA performance can be improved. Therefore, this study can be considered a starting point for a future validation study of this new method conducted on larger fMCG data sets affected by fetal movements.

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ID 421015

Open Architecture Software Platform for fMCG Data Analysis

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Multichannel signal analysis is a key procedure in fetal magnetocardiogram (fMCG) studies. This task is often accomplished by custom designed software with limited functionalities for a specific application. This work proposes an open architecture software platform to allow analysis tool building as plugin components. Plugins are software components automatically connected to the platform. We have already incorporated in this platform, linear and nonlinear analysis methods that provide fMCG signals basic analysis, independent component analysis [1], a third party flexible graphic visualization module [2], and basic input/output support.

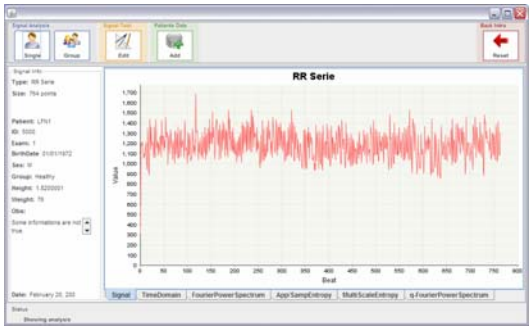

Fig. 1 – Software interface

The software platform is engineered in such way that allows rapid easily extensions of its functionalities. This had been proved to be a very fast and practical way to construct new analysis methods. Another interesting feature of this platform is its operating system independence; therefore it works in most computer architecture and operating systems. The basic platform of this software was programmed in Java language, so that it needs Java environment to run [3]. Java environment supports real time component loading, therefore a new plugin placed in a specific directory is automatically loaded and ready to use. The graphical user interface of this software is illustrated in ***Fig. 1*** showing a time series and basic statistical analysis for a signal. We propose a growing collaborative expansion of this software which basic version with the above functionalities will be freely available in open source. This software platform has potential to evolve to flexible high sophisticate analysis software adaptable to various applications.

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Correlation of Linear and Non-Linear Parameters on fetal Magnetocardiograms

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The assessment of fetal well being without using invasive methods is very important. Among non invasive methods, Short Term Variation (STV) [1] analysis has been applied to data collected with cardiotocography (CTG), which uses ultra-sound to extract the fetal heart activity, but had the drawback of a low temporal resolution. Fetal MagnetoCardioGraphy (fMCG) is a another noninvasive method that achieves a much better time resolution. Main works have been published exploring linear and non-linear parameters on fMCG and CTG. Our objective is look for correlations between the main parameters in both linear and non-linear analysis of fMCG data.

In addition to STV, other methods potentially useful to differentiate between healthy and sick fetuses are related to the non-linear entropies analysis. We analyzed the following parameters on fetal traces separated from fMCG recordings using FastICA: STV, LTI and deltaSTV, standard deviation of RR interval series detected automatically, Approximated Entropy (ApE) and Sample Entropy (SE).

Were analyzed 40 records of 5 minutes each, from 14 pregnant women from 21 to 38 week (mean 28 weeks). The records were obtained with a 55 channel SQUID system (ATB Argos 200) in Chieti (Italy), and a 74 Channel SQUID system (Magnes, BTI) in Madison, USA. The Pearson correlation coefficients were obtained for each pairs.

The parameters with the Pearson correlations coefficients are shown in Table 1, with very strong (-), strong (-) and medium correlation (-). As expected, some similar parameters show high correlation, as ApE and SE, mRR and mHR, suggesting that they do not contain any significantly different information. sdRR and deltaSTV (r = 0.90) contain similar information although there is no significant correlation between RR and STV, from which they derive. The non-linear parameters ApE and SE did not show high correlation with none linear parameter, only medium correlation with parameters associated with variability indices such as deltaSTV, mLTI and sdRR. These result suggest that entropy indices contain information about the variability of variation indices.

Table 1

		1	2	3	4	5	6	7	8	9
		ApE	SE	mSTV	deltaSTV	mLTI	mRR	mHR	sdRR	rmsdRR
1	ApE	1.00								
2	SE	0.96	1.00							
3	mSTV	-0.20	-0.22	1.00						
4	deltaSTV	-0.41	-0.41	0.88	1.00					
5	mLTI	-0.44	-0.44	0.69	0.79	1.00				
6	mRR	0.22	0.29	.006	-0.02	-0.19	1.00			
7	mHR	-0.23	-0.29	-0.03	0.05	0.22	-0.998	1.00		
8	sdRR	-0.45	-0.46	0.81	0.90	0.88	-0.19	0.22	1.00	
9	rmsdRR	-0.10	-0.17	0.62	0.70	0.49	-0.19	0.21	0.66	1.00

ID 421017

A possible method to detect synchronization between maternal and fetal magnetocardiograms

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Synchronization appears to be a fundamental principle of nature. It is currently a popular topic of research, partly because of its occurrence in many dynamical systems, ranging from power lines to biological structures. Physiology abounds with examples of such phenomena; just to mention a few: neuronal cells discharge in synchrony; cells in the heart beat together; synchrony in many body biochemical reactions. More specifically, synchronization can be defined as a physical process where two or more appropriately coupled systems undergo similar evolution in time. Mathematically, it may be represented by an asymptotic coincidence of the state vectors of two or more systems. In periodic systems, synchronization is usually described as a phase locking, where the phase difference between the two oscillators is maintained constant. In this framework, previous studies have attempted to apply different approaches in order to evaluate to which level mother and fetus heart beat are coupled and exhibit synchronization [1]. Between all possible techniques to detect heart activity, fetal magnetocardiography (fMCG) has been extensively reported in the literature as a non-invasive prenatal technique that can be used to monitor various functions of the fetal heart. In this work we investigate a method applied to chaotic oscillators to evaluate whether it may be used as a tool to detect phase synchronization between maternal and fetal MCG (2). The proposed algorithm is based on Analytic Signal concept, with which one can determine the instantaneous amplitude [A(t)] and phase [ϕ(t)] of a signal, s(t). An Analytic Signal, ψ(t), of an arbitrary signal s(t), is a complex function of time defined as: $\psi(t) = s(t) + j\check{s}(t) = A(t)e^{j\phi(t)}$, where $\check{s}$ is the Hilbert transform of s(t). We applied the proposed method in 34 concurrent fetal and maternal RR traces, obtained from magnetocardiographic recordings of 7 individuals. Preliminary results show that the method has good temporal resolution to detect periods where maternal and fetus traces are synchronized. This will allow more accurate statistical tests to be implemented in simulated signals as well as in a larger MCG dataset.

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ID 421018

Non linear dynamical analysis of the evolution of the fetal cardiovascular system.

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In the last years fetal magnetocardiography (fMCG) has been used to detect fetal cardiac activity at different gestational ages, and the independent component analysis (ICA) has been applied in reconstructing reliable fetal cardiac signals [1]. In the framework of non linear dynamical analysis, entropy estimators, such as approximated and sample entropies, have been adopted to develop an entropy-based method for the automated categorization of independent components separated with ICA from fMCG [2] and to characterize the rate of variability of both fetal and maternal cardiac signals. A more detailed study on the dynamical properties of the fMCG signals have been recently started in order to achieve a simple theoretical model describing the main characteristic of the experimental data. The estimation of the correlation dimension [3] and of the distribution of the Lyapunov exponents [4] give informations on the eventual deterministic nature of the system and on the number of degrees of freedom involved in the collected experimental data.

The main results of our analysis can be summarized as follow: (i) the phase plot analysis reveal a gestational age dependent change of the fetal trace; (ii) there is no particular difference between the correlation dimensions of the maternal and fetal traces, which reflects that the same dynamical model could be used for both maternal and fetal hearts; (iii) the spectra of the Lyapunov exponents for maternal and fetal traces at different gestational age reveal the deterministic nature of the systems; (iv) the dynamical model suggested by our results should be composed of a low number of coupled oscillators in agreement with previous findings; (v) the differences observed in the maternal and fetal cardiovascular systems account for different parameter values in the equations of the coupled oscillators.

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ID 421019

Fetal Magnetocardiography in Multiple Pregnancies

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Common to most life-threatening advanced disease states in the fetus are disturbances in conduction and repolarization, usually evaluated on the basis of Cardiotocography (CTG) and surface Electrocardiography (sECG) during gestation. CTG uses ultra-sound technology to estimate fetal heart activity but it has limited time resolution. sECG, detected from the surface of the maternal abdomen, has high temporal resolution but is affected by disturbances due to the effect of the insulating properties of fetal and maternal tissues. Fetal Magnetocardiography (fMCG) overcomes this limitation while preserving an excellent time resolution (1 ms). Independent component analysis (ICA) of fetal magnetocardiograms permits to obtain fetal cardiac signals on which the QRS complexes, and often also the P and T waves, can be recognized. Disturbances such as arrhythmias, T wave alternans or QT prolongation, can then be evaluated prenatally.

For the fetuses of the multiple pregnancy, the risk of prenatal morbidity and mortality is even higher. In an effort to better understand the causes of fetal demise, an international consortium of researchers (Chieti University – Italy, and University of Wisconsin at Madison – USA) collaborated to analyze fMCG from multigestational pregnancies. Twelve multiple pregnancies (2 triplets, 10 twins) were referred because of suspected fetal arrhythmias, growth restriction, and presumed normal multigestation pregnancy. fMCG data were recorded using a 55-channel magnetometer ATB system (University of Chieti), and a 37-channel first-order gradiometer system (University of Wisconsin-Madison). When possible, fMCG were recorded several times along gestation. A total of 41 fMCG data sets (15 for triplets, 26 for twins) recorded from 20 to 37 weeks were processed with FastICA algorithm.

In one triplet we could separate the signals of all fetuses using a single data set only at 30 weeks gestation, whereas an additional data sets was used for the data at 24 and 28 weeks. In the other triplet, the fetal signals were separated using a single data set at all gestational ages (24, 25 and 26 weeks). In the latter case, we could detect rhythm disturbances in one fetus at 25 and 26 weeks.

In the twin pregnancies, the cardiac signals were reconstructed in 12 out of 26 data sets for both fetuses, and in 12 out of 26 data sets for one fetus. No correlation with gestational age was observed. In 5 out of 7 arrhythmic pregnancies, it was possible to separate the cardiac signals from both fetuses.

These results demonstrate that ICA processed fMCG data sets can contribute in defining high risk states in the human multiple pregnancy and in linking disturbances in cardiac conduction and repolarization to fetal outcome.

ID 421020

Fetal dysrhythmias – a clinician's viewpoint

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The diagnosis of fetal cardiac dysrhythmias and structural malformations of the fetal heart has been revolutionised by the application of fetal ultrasonography. While structural defects and their hemodynamic consequences can be visualised real-time, information concerning fetal arrhythmias is inferred from the fetal heart rate, and the relationship between atrial and ventricular mechanical events as demonstrated by M-mode echocardiography and Doppler flow signals from the atrioventricular and arterial valves. Fetal ultrasonography has proved to be a vital clinical tool in the diagnosis and sequential follow-up during pregnancy of fetuses with a variety of dysrhythmias.
The fetal magnetocardiogram (fMCG) can be reliably recorded from approximately the 15th week of gestation onwards. The fMCG records the magnetic field generated by electrical activity of the fetal heart, and as it is generated by the same sources as for the ECG the recorded complexes will have the typical morphology of the P wave, QRS complex and T wave with sufficient accuracy from about the 20th week of gestation onwards, to allow precise diagnostic evaluation of fetal cardiac dysrhythmias.
Issues of cost, ease of use and portability have to be resolved, if the fMCG is to move from the laboratoy to the bedside. In the meanwhile, its application in selected groups of patients at risk of potentially lethal arrhythmias will provide clinically useful data, and should form the basis for diagnostic and therapeutic trials.

ID 421021

Sudden Death before Birth in the Fetus with Ebstein's Anomaly or Tricuspid Valve Dysplasia

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Background: The fetus with anatomical abnormalities of the tricuspid valve causing severe insufficiency and right atrial enlargement has one of the highest incidences of in utereo demise of all fetal cardiac disease. We hypothesized that in utero demise is due to arrhythmia, and fetuses at risk of imminent death could be detected by fMCG.

Methods: Using a 37 channel biomagnetometer, we evaluated 11 fetuses with either Ebsteins anomaly of the tricuspid valve, or tricuspid dysplasia at 24 -32 weeks of gestation. Baseline rhythm, heart rate variability, cardiac intervals and p-QRS morphology were determined during 5-7 10 minute periods per patient. Outcome of pregnancy (stillbirth, live birth) and postnatal survival or non-survival was assed by chart review.

Results: Data was successfully attained on all patients. Three had normal findings: one is still in utero, one was live-born at term, the other developed hydrops 6 weeks after the fMCG, was delivered at 34 weeks. Abnormal findings included: a prolonged PR interval in 4 pts, prolonged QRS (from 84-125 msec, nl < 50 msec) and/or p-wave duration in 6 pts, and large amplitude p-waves and/or QRS complex in 2 pts. No pt had WPW. Two patients died in utero between 33-34 weeks, and additional mother underwent emergency c-section for loss of fetal heart tones but the baby could not be resuscitated. The fMCG findings in these 3 pts were noteworthy: all had decreased HR variability, and all had prolonged and deep decelerations. The rhythm during the decelerations was not sinus, but type 2 2° AV block. All 3 died within 2 weeks of this finding. Of the initial 11 pts, 3 survived long-term, and one is still in utero.

Conclusions: The rhythm during deceleration in pts with tricuspid valve disease is not due to sinus bradycardia, but AV block, and may be the mechanism of sudden death. The clinical findings of decelerations and poor heart rate variability should prompt timely delivery in these very high risk fetuses.

ID 421022

Determination of fetus gender by using BI-DIGITAL O-RING test

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Introduction and Aims: Bi-Digital O-Ring Test (BDORT), established and developed by Prof. Y. Omura as non-invasive diagnostic method, may be very useful in fetus gender determination.The aim of the study was to evaluate the accuracy of BDORT in determination of fetus gender and to compare the results obtained with standard methods applied in perinatology.

Material and Method: 149 pregnant women were examined by indirect BDORT. Slides with human sexual chromosomes were used as referent substances: XX and XY. 15 pregnant women, between 6th and 11th week of gestational age, were examined prior chorionic villi biopsy and genetic analysis. 134 pregnant women, between 18th and 36th week of gestation, were examined by ultrasonography in order to determine fetus gender. The results obtained from indirect BDORT were compared with the fetus gender following delivery.

Results and Discussion: The same results of gender determination were obtained by using both BDORT, on one side, and by chorionic villi biopsy and genetic analysis, on the other in vast majority of cases. The diagnosis was missed in three cases and some peculiar information was obtained in five cases. When test is performed by using both slides (XX and XY), the test results were negative. The same results of gender determination by using BDORT on one side and standard methods on the other, were obtained in 94.63%.

Conclusion: This study results indicate that indirect BDORT may be applied as a screening method to determine fetus gender. This fact will raise the other issue, namely, whether indirect BDORT may be applied in screening of various genetic syndromes and genetic diseases when slides, with the proper referent substances, are used.

ID 421023

Classification of AF type using Magnetocardiographic analysis

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Background: Magnetocardiography (MCG) is a new, totally non-invasive, non-contact and highly sensitive method to detect atrial F-wave in AF patient than ECG. K. Kornings and M. Guillem reported three types of AF- single broad wave front, one or two wavelets, and highly fragmented wavelets, using 244 and 56 electrodes based on the complexity of atrial activation. MCG gives a good help to define the F-wave type easily.
Methods: To detect weak atrial excitation, we utilized a high sensitive low-Tc 64-channel MCG system with application software KRISSMCG64. According to the F-wave activity size criteria (0.1 pTesla), we classified AF as type I (more than 0.1pT) and type II (less than 0.1pT). And we conduct the minimal AF surgery in twelve AF patients. Their mean age is 65±9 years old (range; 46-77), 75% male (9/12), 83% chronic AF (10/12), 67% structural heart disease (8/12), LA size is 56±12 mm (range; 45-80) and AF duration 17 months. Monthly-based ECG was used for follow-up.
Results: Type I is 58% (7/12) and type II is 42% (5/12). Overall AF free rate is 75% (9/12) at postop, 44% (4/9) at discharge, 71% (5/7) at 3 months, 83% (5/6) at 6 months, 100% (5/5) at 9 months, 100% (5/5) at 1 year, 100% (3/3) at 1.5 years, 100% (2/2) at 2 years, and 100% (1/1) at 2.5 years. Follow up duration is 10 ± 11 months (range; 0-32). We have one rhythm-related death (stroke), and two non-rhythm-related deaths (CRF sepsis and heart failure). There is 75% (9/12) anti-arrhythmic drug-off and no sick sinus or no permanent pacemaker insertion. Type I has 71% (5/7) AF free rate and type II 80% (4/5) success rate.
Conclusions: Classification of AF type based on MCG analysis does not affect the success rate between two groups. MCG map-guide might be a new and feasible method. MCG might be a new and feasible method to analyze AF.

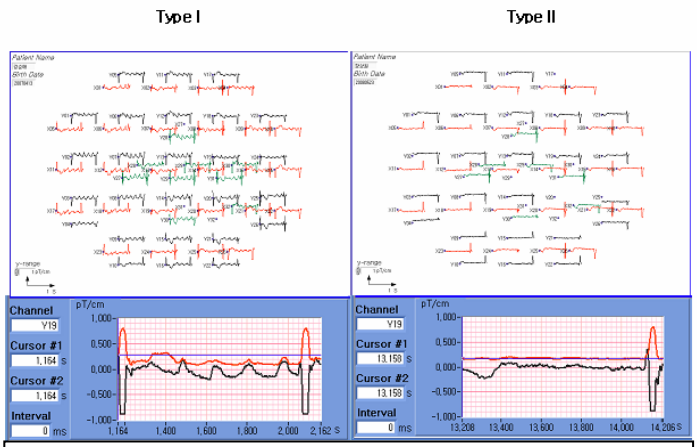

Figure 1. AF type according to the amplitude (0.1 pT) and duration (20 ms) of F-wave activity from the MCG system. We classified F-wave as type I (bigger than 0.1 pT and longer than 20 ms) and type II (smaller than 0.1 pT and shorter than 20 ms).

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ID 421024

Magnetocardiography Map Guided Minimal Atrial Fibrillation Surgery in Patients Who Having Long-standing Persistent AF And Structural Heart Disease

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AF is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function. On the electrocardiogram (ECG), AF is described by the replacement of consistent P waves by rapid oscillations or fibrillatory F waves that vary in size, shape and timing, associated with an irregular, frequently rapid ventricular response. AF is the most common clinically significant cardiac arrhythmia, accounted for 34.5 % of patients hospitalized with a cardiac rhythm disturbance. The prevalence is estimated at 1 % of general population, but increasing rapidly with age. Two million Americans and 4.5 million Europeans are suffered now, and the projected number of patients will reach double within 30 years. However, millions of patients remained untreated. Only 3 % of the AF patients are treated by EP ablation or Maze operation, and 97 % remained with/without anticoagulation medications. So, millions of AF patients are at risk for stroke and embolism. AF classified as paroxysmal, persistent and longstanding persistent according to the duration and self-termination. Conventional ECG is insufficient to localize AF focus in atrium, only give whether AF or not. Therefore, now we conduct AF treatment without map in surgery or very limited map in EP ablation. EP study is very invasive, one and more hours needed to conduct, moderate x-ray hazard, hard to both patient and physician, so only the patient who have normal size heart and tolerable LV function endures the total EP procedures. Success rate of EP ablation remains at 70-80 % in paroxysmal, 50-70 % in long standing persistent AF. In 1990s, Cox et al developed a surgical procedure that controls AF in more than 90 % of selected patients. Although the Maze procedure is effective, the complexity, long incision length, prolonged CPB time, and bleeding risk prevented widespread application. AF surgery is now conducted as an adjuvant combined procedure when the patient underwent main operations for structural heart disease, such as valvular replacement or coronary bypass. Still lone AF surgery for normal heart condition is not accepted yet because of its burden of full lesion set of Maze procedure. Basically, Maze is not a map-guide surgery, so it might have unnecessary incisions. If we make a personalized F-wave map, we minimize the lesion set and conduct easily.

Magnetocardiography is very sensitive method to detect F-wave with high accuracy and much information from 64 channels. It is non-contact, non-invasive, x-ray hazard free, easy and physiologic tool. Home-made KRISSMCG64 software algorithm helps localize F-wave action potential activity in spatio-temoral scale. Combining individual CT image with MCG records, we make a personalized F-wave map in 3D heart surface model. By this, we tested 28 patients' F-wave including paroxysmal, longstanding persistent, wandering pacemaker patients. Among them, 12 cases were successfully analyzed to make F-wave map. 8 patients are open cardiac surgical candidate having structural cardiac disease to be corrected with long standing persistent AF and others are paroxysmal AF or non-cardiac disease patients. Mean age is 63 years old, AF duration is 17.3 months, AF burden is 1.0, LA size is 60.3 mm, LVEF is 54.3 %. We use cut-and-sew and cryo ablation. We have two op mortalities, one is CRF sepsis and the other is stroke. AF free rate is 88 % (7/8) at postop, 83 % at 3 months (5/6) and 6 months (5/6), 100 % at 9 months (5/5), 1 year (5/5), 1.5 year (3/3), 2 year (2/2), and 2.5 year (1/1). There are no sick sinus syndrome, no permanent pacemaker insertion. Drug-off rate and recur free rate are 100 %. Using MCG map-guide, we can minimize AF surgery instead of full Maze procedure and it might be a new method to treat AF.

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ID 421025

Whether BI-DIGITAL O-RING Test can improve perinatal outcome?

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Introduction and Aims: Bi-Digital O-Ring Test (BDORT), developed by Prof. Y. Omura as non-invasive diagnostic method, may be very useful in perinatal diagnosis. The aim of this paper is to show whether BDORT can be used as diagnostical method which can detect the perinatal disease at early stage and, therefore, be used as a routine method for screening.

Material and Method: Pregnant women were examined by indirect BDORT. Different diagnostic slides were used as referent substances.

Results and Discussion: BDORT showed infection of pancreas in 9 out of 128 pregnant women. The OGTT was positive revealing glucose intolerance in 8 patients (89%). In one patient, BDORT revealed asymptomatic infection with Toxoplasma gondii. This result was confirmed by routine blood analysis showing increased IgM level.

Conclusion: Regarding pancreatic infection and ACh, BDORT showed that, besides normal fasting blood glucose level, certain changes in sugar metabolism may be present and, whether ACh is lowered, 3-hour OGTT is recommended. By referring to lab patients with normal fasting blood glucose level and lowered ACh level, physicians may reveal patients with glucose intolerance and preventive measures may be applied (appropriate diet, physical activities, more frequent check-ups of woman and fetus etc.). Generally, by using indirect BDORT as non-invasive and safe method in pregnant women, physicians may detect asymptomatic infections (such is Toxoplasma gondii infection) and changes (such is glucose intolerance) which, in turn, may result in adequate approach to each patient. This will enable a wide range of preventive measures to be undertaken and, in that way, the onset of certain diseases will be prevented

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Maturation of the autonomic nervous system under the influence of placental insufficiency

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Motivation: The aim of this study was the evaluation of the autonomic nervous regulation in intrauterine growth restriction [IUGR]. Fetal beat-to-beat heart rate variability [fHRV] was applied using longer monitoring intervals than the previous 256 beats, the more recently proposed specific fetal frequency bands and taking into account gestational age [GA] and fetal activity.

Methods: 16 fetuses with IUGR (ultrasound: weight < 10th perc.; increased resistance indices in uteroplacental perfusion, 2 with a brain-sparing effect) were matched to normal controls and stratified by GA: (1) < 29+0; (2) 29+0 to 32+6; (3) >= 33+0 weeks. FMCGs were recorded continuously over 30 min by an ARGOS 200 multichannel-magnetometer-system (AtB) in a shielded environment. The data were preprocessed offline and from the visualized heart rate trace an estimate of the fetal activity levels was made. Segments of at least 10 min of fetal quiescence were chosen, 5 min were used to compute the following fHRV parameters: mHR, SDNN, RMSSD, SDNN/RMSSD, feHF, feLF, feVLF, feVLF/feHF, feVLF/feLF, feLF/feHF (2).

Results: There were no significant differences between subjects and controls in groups (1) and (3). Between 29-33 weeks GA IUGR fetuses showed a significantly higher ratio of feVLF/feHF (p= 0,016) and a trend to higher SDNN/RMSSD (p= 0,117; both Mann-Whitney-U).

Discussion: Our results hint a critical interval between the 29th and 33rd weeks GA for the development of the autonomic nervous system. Results from previous studies could be confirmed for longer time series, that IUGR seems to be associated with higher sympatho-vagal balance depending on the time of diagnosis and hence severity of the problem. We can confirm that the frequency domains of fHRV suggested by David et al. 2006 appear more suitable for fetuses than those defined for adults.

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Atomic magnetometer: non-cryogenic technology for biomagnetism

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Biomagnetism measurements and the data processing for source localization and imaging require, besides high sensitive magnetic field measurements, a large number of measuring sites. Fast data acquisition from multiple sites is necessary in monitoring a dynamic source. In the last decades the only technology capable of biomagnetism measurements is the cryogenic low-T_c superconducting quantum interference device (SQUID) magnetometers. Lately, a novel atomic magnetometer has achieved a record magnetic sensitivity and source localization accuracy [1]. In an atomic magnetometer high density alkali vapor (K, Cs, Rb) is generated in a glass cell by warming it up. By a process known as *optical pumping*, the *spins* (magnetic dipoles) of the alkali atoms are aligned along an incoming circularly polarized laser beam tuned to a specific atomic transition. A magnetic field perpendicular to the pump beam rotates the spins by a small angle proportional to the field magnitude. This angle is measured by the polarization rotation of a laser probe beam. The magnetometer sensitivity is limited by spin-alignment relaxation due to collisions of the alkali atoms with buffer gas atoms, with the walls of the cell, and with one another. The latter, known as spin-exchange relaxation, is the main sensitivity-limiting factor. This phenomenon is almost completely eliminated in a *spin-exchange relaxation-free* (SERF) atomic magnetometer by using a high-density alkali vapor in a very low magnetic field along with a high pressure buffer gas which prevents diffusion to the walls. Due to this high-pressure buffer gas, the diffusion of the alkali atoms is drastically reduced and the spin rotation is affected by the local magnetic field only. Thus, any small volume in the cell, a "voxel", measures the local magnetic field [2]. The SERF atomic magnetometer is capable of multi-channel operation, gradiometer operation and multiple sites 3D measurements of the magnetic field inside a single vapor cell. Although the sensitivity of an atomic magnetometer relates to the number of alkali atoms in the measuring volume, its high sensitivity allows to reduce the measuring volume down to a few mm^3, keeping a measurable signal-to-noise ratio. We trade a part of the sensitivity to local measurement of the magnetic field. Operating in a gradiometer configuration, the sensitivity threshold of the SERF atomic magnetometer was shown to be better than 0.5 fT/√Hz for a 0.3 cm^3 measurement volume, adequate to high-sensitive biomagnetism. Signals from the heart and brain have been recorded for the first time with a non-cryogenic magnetometer [3].

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ID 421028

Magnetocardiography in the Fetus with Rhabdomyoma

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Background: Cardiac rhabdomyomas have been associated with bizarre ECG findings and multiple arrhythmias in the postnatal patient. We wondered what unusual rhythm findings would be seen before birth.

Methods: We evaluated 8 fetuses from 20-36 weeks with single or multiple cardiac rhabdomyoma referred from multiple perinatal centers in Illinois and Chicago. Using a 37 channel biomagnetometer, we assessed baseline rhythm, heart rate variability, cardiac intervals and p-QRS-T wave morphology during 5-7 10 minute periods per patient. Postnatal outcome was assessed by chart review.

Results: Of the 8 patients evaluated, 3 (a set of twins and a singleton with a large LVOT tumor) had completely normal findings. One with a RA tumor had junctional ectopic tachycardia which was successfully treated with digoxin in utero and after birth. Atrial ectopy was noted in 2 pts. Other findings included a WPW-like pattern, bi-directional QRS complexes, and wide and bizarre QRS morphology. The PR interval was variable, short in some and long in others. All fetuses survived to be live-born, 2 had tuberous sclerosis. One without SVT in utero developed SVT after birth and required antiarrhythmic treatment.

Conclusion: In this case series more than half of the pts showed bizarre fMCG findings, some of which have not been seen in postnatal life. Sustained arrhythmia can develop after birth even without manifesting itself in prenatal life.

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Perinatal Biomagnetism 2009: how can it help sick fetus/infant?

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