The Effect of Different Electrode Design on the Electrohysterogram Signal

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Áhrif mismunandi rafskauta á legrafritsmerkið

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Útdráttur

Inngangur

Legrafrit (*e*. electrohysterography, EHG) er tækni sem mælir rafvirkni í legvöðvanum og er hægt að beita til að mæla hríðir. Vonir standa til að með þessari tækni megi betur greina hvort um alvöru fæðingahríðir sé að ræða eða einungis samdrætti sem ekki leiða til fæðingar. Rannsóknarhópar víða um heim vinna að þróun legrafritstækni en misræmi er talsvert í birtum niðurstöðum þeirra, hugsanlega vegna mismunandi rafskauta sem notuð eru við mælingarnar. Rannsóknin fólst í samanburði á þrenns konar rafskautum til að kanna hvort munur væri á merkinu sem þau gefa frá sér við mælingu samdrátta. Einblínt var á tíðnieiginleika merkisins. Einnig var kannað hvort að staðsetning rafskauta ofan eða neðan nafla hefði kerfisbundin áhrif á ritið.

Efniviður og aðferðir

Tíu konur í framköllun fæðingar á Kvennadeild Landspítalans í mars og apríl 2015 tóku þátt og voru legvöðvasamdrættir þeirra mældir með legrafritun auk venjulegs hríðamælis í u.þ.b. 30 mínútur. Mæld voru merki frá leginu í 39 samdráttum. Þrjár gerðir rafskauta voru bornar saman við mælingarnar, tvö rafskaut af hverri gerð. Engum persónuupplýsingum um þátttakendur var safnað.

Niðurstöður

Mælingarnar sýndu að mikill breytileiki var á mæligildum samdrátta hjá sömu konu og einnig milli kvenna. Þessi breytileiki var mun meiri en breytileiki merkisins milli rafskautategunda. Ekki mældist marktækur munur á legrafritsmerkinu vegna mismunandi staðsetningar og var munurinn hverfandi miðað við breytileika milli kvenna og samdrátta.

Ályktanir

Með þessari rannsókn var ekki sýnt fram á að gerð rafskauta hefði afgerandi áhrif á tíðnieiginleika legrafritsmerkisins. Þar sem munur á milli rafskauta er lítill í samhengi breytileika milli samdrátta benda mælingar til þess að gerð rafskauta sé lítill áhrifavaldur í mismun í birtum niðurstöðum fyrir þessa tegund merkja. Því má færa rök fyrir því að nota megi þau rafskaut sem henta best hverju sinni án þess að það hafi áhrif á gæði mælinganna. Ekki var hægt að sýna fram á marktækan mun milli mælinga ofan og neðan nafla og ætti því almennt ekki að skipta máli á hvorum staðnum er mælt.

The Effect of Different Electrode Design on the Electrohysterogram Signal

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Abstract

Introduction

Electrohysterography (EHG) measures the electrical activity in the uterus and can be used to analyze labor contractions. One of the goals of EHG development is to use it to discriminate true labor contractions from contractions that will not cause birth. Different research groups around the world have been working on EHG but considerable inconsistency is between published results from different research groups, possibly because they use different types of electrodes for their measurements. This work compared three different electrode types to determine if and how the EHG signal differs between them and also if electrode location above vs. below the umbilicus has effect on the signal. In this work only the difference in frequency properties of the signal were studied.

Material and methods

Ten women undergoing induction of labor at Landspitali participated and were measured with EHG and tocodynamometer simultaneously for approximately half an hour, 39 contractions were observed. Three different electrode types were compared, one of each type above and below the umbilicus. No personal or medical data about the participants was gathered.

Results

The measurements showed a great variability in values between contractions, intra- and inter-subject. This variance was considerably greater than the difference possibly caused by electrode type. No significant difference was found between the same electrode types above and below the umbilicus and this difference was much smaller than the variability between contractions.

Conclusions

This study did not find a significant contribution of electrode type on the frequency parameters of the EHG signal from contractions. Because the difference between electrode types is small compared to the normal variability of the signal electrode type does not appear to be a determining factor in the divergent results from different research groups. The variability between the frequency parameters of the contractions is much larger than the difference caused by difference between locations. Locations of electrodes above vs. below the umbilicus did not show significant difference and seems not to be of any great importance to the signal observed.

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Abbreviations

Ag/AgCl	Silver/silver chloride
ECG	Electrocardiography
EHG	Electrohysterography
EMG	Electromyography
F10	10% limit frequency
F50	Median frequency
F95	95%limit frequency
FW_H	Fast wave high
FW_L	Fast wave low
MPF	Mean power frequency
PDS	Power density spectrum
PEAK	Peak frequency
TOCO	Tocodynamometer

1. Introduction

1.1 The pregnant uterus

The uterus is located in the female pelvic cavity in the midline between the bladder and rectum. It is a thick-walled muscular organ made of smooth muscle lined with the endometrium and coated by serosa. The muscular wall is heterogeneous and is composed of an outer longitudinal layer and an inner circular layer. The role of the uterus is to protect and foster the fetus and ultimately expel it at birth (1-3).

The uterus consists of a body (corpus) and a cervix. The uppermost part of the corpus, the fundus, communicates with the fallopian tubes on either side while the cervix is placed inferiorly and opens into the vagina (2, 3).

The uterine smooth muscle is built up by myometrial cells and uterine contraction is a direct consequence of the underlying electrical activity of those cells. The connection between contractions and electrical events has been demonstrated by isolated myometrial tissue studies (4). The smooth muscle´s contractile unit contains thin actin and thick myosin filaments as well as the regulatory protein calmodulin which initiates contraction by activating the myosin cross bridges (5, 6).

Spontaneous electrical activities in the muscle are composed of intermittent bursts of spike action-potentials. This is initiated by stimuli such as hormones (mainly estrogen) and increased stretch on the muscle. Single spikes are sufficient to start contractions but in order to maintain powerful contractions multiple, synchronized, higher-frequency spikes are necessary (4).

The resting potential of a membrane is the difference between the negative inside and the positive outside potential of a resting membrane and is directly related to calcium, potassium and chloride ion concentrations within the cell and in its environment. It is difficult to give resting potential an absolute value in uterine smooth muscle cells because of its slow sinusoidal fluctuations but in pregnant women it usually ranges from -80 to -65 mV compared to action potentials of around 12 to 25 mV (6). Changes in resting membrane potential is principally caused by opening of voltage dependent Ca^{+2} L-type channels caused by the aforementioned stimuli. This leads to increased intracellular Ca^{+2} concentration and the forming of a Ca^{+2}-calmodulin complex. Although most of the calcium ions that cause contractions are originated in the extracellular fluid some come from the sarcoplasmic reticulum of the cell. The Ca^{+2} -calmodulin complex then activates myosin light chain kinase that phosphorylates the myosin light chain resulting in a muscular contraction (4, 5).

The frequency, amplitude, and duration of contractions are primarily determined by the frequency of occurrence of the uterine electrical bursts, the total number of muscle cells simultaneously active during the bursts, and the duration of the uterine electrical bursts. Each burst stops before the uterus has completely relaxed (4).

Myometrial cells are linked together by gap junctions composed of connexin proteins. Gap junctions are intercellular channels that allow passage of inorganic ions and small molecules. Throughout pregnancy these cell-to-cell contacts are low but hormonal changes before delivery

causes them to increase, forming an electrical syncytium necessary for coordination of myometrial cells and effective contractions (4, 6).

1.2 Preterm birth

Normal labor takes place in term pregnancy, i.e. between 37 and 42 weeks of gestation but labor occurring before this time is defined as preterm. Preterm birth is further subcategorized: (A) extremely preterm birth is before 28th week of gestation, (B) very preterm birth is between 28th and 32nd week of gestation and (C) moderate or late preterm birth if happening during 32nd to 37th week (7). The shorter the pregnancy the greater the risks of fetal death and complications (3).

1.2.1 Preterm birth worldwide

About 10% of newborns worldwide are preterm infants, which is about 15 million newborns each year. Births occurring before 32 weeks of gestation age account for about 1% of all births (8). Preterm birth and its complications are the cause of death of almost 1 million children yearly making it the leading cause of death in children under the age of five. The surviving preterm infants often face serious disabilities such as hearing and visual problems, learning disabilities and chronic lung disease. Moreover preterm birth accounts for up to 50% of cerebral palsy (3, 7).

Although over 60% of preterm birth take place in South Asia and Africa the problem is in fact global. The rates for preterm infants are 12% in lower-income countries compared to 9% in higher-income countries and the rates are increasing. In general, poorer families are at greater risk within countries (7).

1.2.2 Preterm birth in Iceland

Compared to other high-income countries preterm birth rates in Iceland are low, about 6%. In the years 2009-2013, 28.090 children were born in Iceland. 1667 of them were born before 37 weeks of gestation, thereof 211 multiples. 264 of those preterm infants were born before 32 weeks of gestation (thereof 29 multiples). Of all preterm neonates nine died during their first week of life and three 8-365 days after birth (9).

1.2.3 Causes of preterm birth

Although preterm labor is sometimes induced by medical means (iatrogenic) most happen spontaneously. Preterm birth has various known causes such as cervical incompetence, multiple pregnancies, maternal diabetes and high blood pressure. Genetic influence also plays a role but often no cause can be identified (7, 10).

No treatment to effectively stop preterm labor has yet proved successful but early diagnosis is considered crucial. Atosiban, an oxytocin antagonist, can delay birth in preterm labor giving an

important timespace to prepare the premature fetus for extrauterine life. Several techniques to diagnose and monitor labor have been adopted but are all subjective or indirect and do not provide a precise prediction of when labor will take place.

1.2.4 Progesterone

The hormone progesterone is essential for a successful pregnancy. It is secreted in large quantities by the placenta in an increasing amount during the course of pregnancy. It suppresses a number of genes essential for effective uterine contractions e.g. genes for the gap junction protein connexin 43, calcium channels and oxytocin receptors. Progesterone also upregulates generation and action of cAMP and cGMP, a part of the relaxation mechanisms as well as competing with estrogen (estrogen increases myometrial contractility) (5, 11).

Synthetic progesterone, progestin, is a promising approach to both preventing preterm labor initiation as well as treating one that has already started. Progestins are a group of steroid hormones including natural progesterone and its analogs, e.g. 17 alpha hydroxyprogesterone caproate and medroxyprogesterone acetate (8). Many questions regarding this subject remain unanswered, such as optimal progestin formula, route, dose and timing of administration.

1.3 Induction of labor

Labor can be induced i.e. started artificially, on medical indications, most commonly because of a prolonged pregnancy (41 weeks or more). Theoretically, induction is performed when continued pregnancy exposes the fetus and/or mother to a greater risk than the induction itself. However this is not always the case in practise as estimating those risks can be impossible. Besides prolonged pregnancy, there are many other indications for induction, such as suspected intrauterine growth restriction, antepartum haemorrhage, pre-eclampsia, maternal diabetes, hypertensive disorders or cholestasis, fetal death in utero as well as social reasons (3, 12, 13).

Induction is usually performed using vaginal prostaglandin E_2 which starts labor or softens, dilates and effaces the cervix allowing amniotomy as the next step. If the desired effect is not gained by one dose, prostaglandin administration can be repeated several times by 4-6 hours intervals (12).

If the cervix is ripe, labor can be induced by amniotomy as a first step. Then the fetal membranes are ruptured with an amniohook or some sharp instrument. If labor has not begun two hours later, oxytocin infusion is started (3).

Other mechanical methods can also be applied, for example passing a balloon catheter through the cervix and inflating it with saline. Balloon catheter induction is advantagous for women who have a previous history of cesarean section as it avoids potential hyperstimulation and softening of the collagen fibres in the uterine scar which are possible adverse effects of prostaglandins (12). Contraindications (at least relative) for induction of labor are repeated previous cesarean sections and acute fetal distress where cesarean section is indicated (3).

1.4 Monitoring uterine activity

During the course of pregnancy the myometrial cells both proliferate (hyperplasia) and enlarge (hypertrophy). Close to delivery the cells begin to coordinate contributing to synchronized conctractions. Frequently, irregular contractions, called Braxton-Hicks contractions, a physiological phenomenon, start much earlier during pregnancy but these do not lead to delivery (14).

Different methods are used to evaluate pregnancy progression yet none have proved successful in distinguishing between true and false preterm labor accurately. Unnecessary treatment and fewer chances to improve outcome of preterm infants are among the consequences as well as not being able to analyze properly the effects of treatments of preterm labor such as progesterone supplements. This is because some of the cases where treatment seems to work would not have ended in preterm labor at all, giving the therapy a biased result (8). The following methods have been applied to observe pregnancy progression.

1.4.1 Tocodynamometry

Tocodynamometry (TOCO) is a noninvasive technology widely used in everyday obstetrics to determine the frequency and duration of uterine contractions. The equipment consists of a strain gauge placed on the maternal abdomen over the contractile part of the uterus and detects changes in uterine tension. A cardiotocograph is a device used in clinical practice to assess fetal well-being. It is composed of a tocodynamometer and a doppler ultrasound that measures the fetal heart rate (Figure 1).

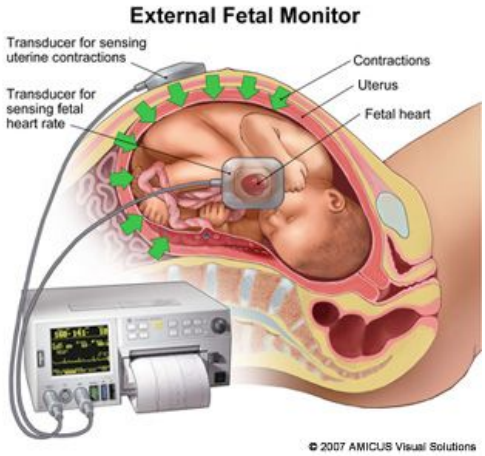

Figure 1. Cardiotocograph. Available at http://www.ginecho.it/monitoraggio-cardiotocografico/ (accessed 11.5.15).

The TOCO measures the external tension of the abdominal wall and identifies the frequency of contractions but does not accurately measure their intensity. The measurement can be affected by

maternal and fetal movements and maternal obesity is a limiting factor with regard to obtaining significant results. Moreover the TOCO needs constant repositioning to work correctly (15, 16).

1.4.2 Intrauterine pressure catheter

Another method, using an invasive intrauterine pressure catheter, does not face those problems and is often considered the gold standard in order to assess uterine activity. However it requires ruptured membranes and introduces risk of infection and placental abruption (16).

1.4.3 Cervical length and fetal fibronectin

Cervical length and fetal fibronectin are birth indicators used clinically. Cervical length is inversely related to the risk of (preterm) delivery and measuring that length by transvaginal ultrasound can identify women at risk for preterm labor.

Fetal fibronectin is an extracellular matrix glycoprotein produced by amniocytes and cytotrophoblast. Finding fetal fibronectin in cervicovaginal fluid implies decidual activation. Both those test have low positive predictive values (they do not identify women who are reliably going to deliver preterm) but their values lie in their high negative prediction values (8).

1.5 Electrohysterography

Uterine EMG (electromyography) or EHG (electrohysterography) are synonyms for a noninvasive method that detects electrical signals from the uterus (Figure 2). The method uses electrodes that are applied on the abdominal surface over the pregnant woman´s uterus and identifies electrical activity and thereby contractions in the myometrium (6). Apart from being able to detect contractions better than TOCO, maternal obesity has less effect on the EHG (15, 16). Numerous studies have analyzed the EHG recordings associated with pregnancy and preterm labor and EHG is potentially the best predictor of preterm labor (17).

The EHG signal can be categorized into two different frequency areas. A low frequency area around 0.005 Hz, with a period equal to the duration of a contraction and a fast wave frequency superimposed on the low frequency wave. The fast wave band is directly related to cellular activity and represents uterine activity. It can be separated into a low-frequency band (FW_L) 0.2-0.45 Hz, and a high-frequency band (FW_H) 0.8-3 Hz(6). These frequency components may be related to the propagation and the excitability of the uterus respectively (18).

Research on uterine EMG measurements have made some progress towards predicting preterm labor. The EHG signal is different during labor compared to the nonlabor state and experiments have shown changes in certain EHG parameters when true labor takes place (8). Assessments of EHG signals might help to answer questions regarding progesterone administration contributing to a effective prevention and treatment of preterm labor (8).

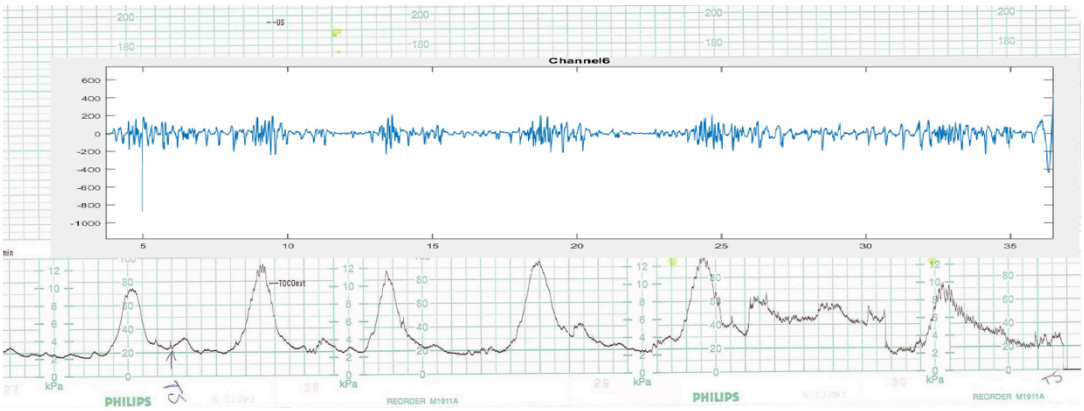

Figure 2. Signal from TOCO (below) where spikes indicate contractions. The EHG signal is superimposed.

1.5.1 EHG parameters

Various parameters can be calculated from EHG signals and are widely used in studies on pregnancy monitoring and preterm delivery prediction. Frequency-related parameters are well suited for quantifying EHG signals (17). Spectral changes have been reported for the EHG from lower frequency contractions during pregnancy to higher frequency at parturition (19).

The power density spectrum (PDS) curve is a function of frequency and represents the relative contribution of each frequency to a signal. The PDS curve of a signal can be used to calculate various parameters of that signal (17).

Mean frequency

Mean power frequency (MPF) is calculated as the sum of the product of the power spectrum intensity and the frequency, divided by the total sum of the intensity of the PDS.

$$\text{MPF} = \frac{\Sigma_i^n I_i f_i}{\Sigma_i^n I_i}$$

Where n denotes the number of frequency components in the power spectrum, f_i the value of the frequency and I_i the intensity of the power spectrum corresponding to f_i.

Peak frequency

Peak frequency (PEAK) of the power spectrum corresponds to the largest amplitude peak of the power spectrum of the EMG signal. It is a commonly used parameter in studies of the uterine electrical activity.

Median frequency

Median frequency (F50) is defined as the frequency where the sums of the parts above and below in the PDS are the same.

95% limit frequency

Comparable to the median frequency, the 95%limit frequency (F95) can be calculated from the PDS. The F95 is the frequency below which 95% of the total energy of the signal is found in the PDS.

10% limit frequency

10% limit frequency (F10) is the frequency below where the PDS contains 10% of the total energy of the signal (17).

Those parameters can be used to help distinguishing between pregnancy and labor contractions. The peak frequency, mean frequency and 95%-limit frequency increase slightly throughout pregnancy but the median frequency tends to be the best parameter for this distinction (17).

1.6 Electrodes

Biopotential electrodes provide an interface between the body and electronic measuring apparatus to measure and record potentials and, hence, currents in the body. Therefore they must have the capability of conducting a current across the interface between the body and the electronic measuring circuit. Because the current in the body is carried by ions but by electrons in the electrode and its wire the electrodes have to serve as a transducer, changing an ionic current into an electronic one (20). Different biopotential signals occupy different portions of the frequency spectrum. The main energy of the EHG signal is at the bandwidth 0.1 to 3 Hz compared to a much higher frequency signal from striated muscles and the heart. The ECG (electrocardiogram) e.g. measures signals at a frequency of 0.1 to 500 Hz. Some of the energy of the EHG signal is at a lower bandwidth than 0.1 Hz but bandwidth under 0.033 Hz is most likely caused by mechanical artifacts rather than electrical activity in the uterus(6, 17, 20).

1.6.1 Polarizable and non-polarizable electrodes

Theoretically, electrodes can be classified into polarizable and non-polarizable electrodes based on what happens to them when a current passes between them and an electrolyte (the conducting gel in this case). No actual charge crosses the electrode-electrolyte interface when current is applied on a perfectly polarizable electrode so the electrode behaves as a capacitor. In a perfectly non-polarizable

electrode the current passes freely across the interface, requiring no energy to make the transition. Neither of these two types of electrodes can be made but some practical electrodes come close to acquiring their characteristics (20).

1.6.2 The silver/silver chloride electrode

The silver/silver chloride (Ag/AgCl) electrode approaches the characteristics of a perfectly non-polarizable electrode and can be made easily. All the electrodes in this study are Ag/AgCl electrodes. They consist of a metal (silver) coated with a layer of a slightly soluble ionic compound of that metal with a suitable anion (silver chloride)(20). Motion artifacts are signals mainly in the low frequency spectrum and are minimal for non-polarizable electrodes, these electrodes are therefore optimal for measuring low frequency signals such as EHG (20).

1.7 Aim of the study

Using EHG measurement for predicting preterm birth is a promising field and is currently studied by different research groups around the world. Although they are often addressing similar problems, a considerable inconsistency is between measurements of the groups, possibly because they are using different types of electrodes. The aim of this BS project was to measure uterine contractions with different types of electrodes simultaneously and to compare the signals attained. The goal was to observe if there was a difference in frequency content in the signals by analyzing the aforementioned parameters (MPF, PEAK, F50, F95, F10) and if different locations of electrodes (above and below the umbilicus) had a significant effect on the signal.

2. Material and methods

The study took place in the Department of Obstetrics and Gynecology at Landspitali National University Hospital in March-April 2015. The subjects were 10 healthy women undergoing induction of labor at term in uneventful singleton pregnancies. EHG was applied with three types of electrodes simultaneously.

The minimum recording time was half an hour but if the women were willing to continue the recording was prolonged to up to one hour. No personal information was recorded and special codes were made for every woman using the letters ISM followed by a three digit sequential number (with leading zeros) e.g. ISM001.

Three different types of electrodes were used in the research; reusable Ag/AgCl electrodes of similar design and identical geometry to those that have been used for the last 10 years in gathering EHG measurements in Iceland (21), single use electrodes that are currently being used to gather a

large database of EHG measurements in Poland and single use electrodes that are used, at Landspitali for routine ECG. Adhesive electrode washers were used to attach the reusable electrodes to the skin and redox electrode gel was applied into them to increase conductivity.

Special snap on cables (TMSi) were used to connect the single use electrodes to the channels of the Porti32 (32-channel ambulatory and stationary signal recorder for physiological researches), the reusable electrodes were also connected to the Porti32. A photo of the setup can be seen in Figure 3.

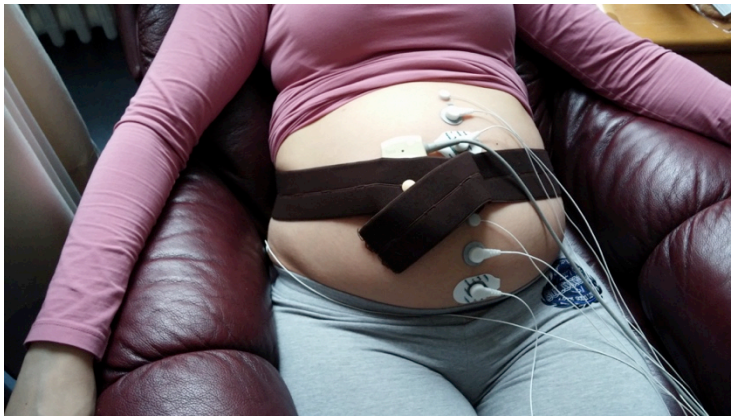

Figure 3. The measurement setup. The tocodynamometer belt passes over the umbilicus.

2.1 The EHG recording protocol

The following measurement protocol was made and used during the study. The protocol was approved by the National Bioethics Committee in Iceland (VSN-15-032) (as can be seen in the appendix). Informed consent was obtained and signed by every woman.

- The women received an explanation about the project, how they would be participating and were informed that they could ask the recording to be stopped at any time and encouraged to notify the researcher if they felt any kind of discomfort during the recording.
- The women were sitting in a reclined lazy-boy chair during the recordings and a blanket was put under their right side to avoid aortocaval compressive syndrome (compression of the abdominal aorta and inferior vena cava by the gravid uterus when the woman is flat on her back).
- The skin was carefully prepared using an abrasive paste and alcoholic solution. The configuration of the electrodes can be seen in Figure 4 and more detailed description can be found in the appendix. Two reusable Ag/AgCl electrodes (patient ground and reference) were attached to the skin over the iliac crests on each side. Six electrodes (two of each type) were attached on the horizontal midline of the abdomen. One electrode of each type was attached above the umbilicus and one electrode of each type under it. The TOCO elastic strap was put

on the horizontal midline over the umbilicus holding the tocodynamometer to one side of the umbilicus. The distance above and below the umbilicus to the active surface (gel) of the first electrode was 3 cm and the space between the active electrode surfaces was at least 5 mm (Figure 5). Figure 5 shows the outer border of the electrodes but the contact areas were smaller for the reusable electrodes (8mm) and the single use electrodes from Landspitali (20 mm).

Electrodes.

ISL	Reusable Ag/AgCl (white)
PL	Single use Poland
LSP	Single use Landspítali

Channel list.

GRD	ISL GND	Left hip
Channel 1	ISL0 (ref)	Right hip
Channel 2	ISL1	1
Channel 3	ISL2	2
Channel 4	PL1	3
Channel 5	PL2	4
Channel 6	LSP1	5
Channel 7	LSP2	6

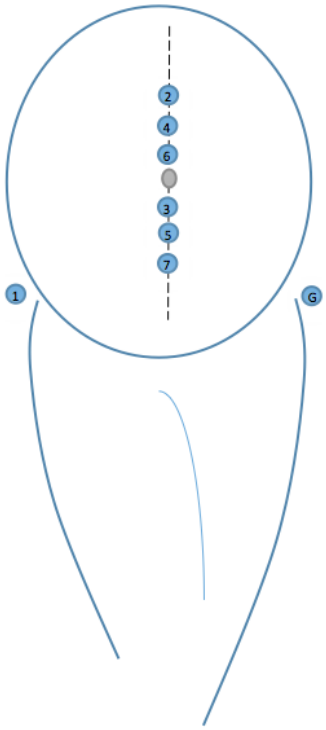

Figure 4. Configuration of electrodes. Numbers indicate the corresponding ports on the Porti32 device.

- The researcher recorded events such as movement or position change of the women and the women were asked to inform the researcher if they felt fetal movements or contractions so they could be recorded.
- The Porti32 device was controlled by TMSi Polybench, a software application toolbox. The signal sampling rate was 256 Hz. To illustrate the recordings in real time a high pass filter with the cut off frequency 0.035 Hz and a 10 Hz low pass filter was used on the signal to give the operator a way of seeing if there was something wrong with any of the electrodes during the measurements.
- The raw unfiltered measurement data was automatically saved in a folder named after the woman´s code (ISMXXX). Three files were saved in each folder; A poly5 file, excel file and a record file. After each measurement the three files were copied and renamed with the

woman´s code. Paper TOCO traces were scanned to several JPEG files and stitched together using ICE panorama generating software (Microsoft ICE).

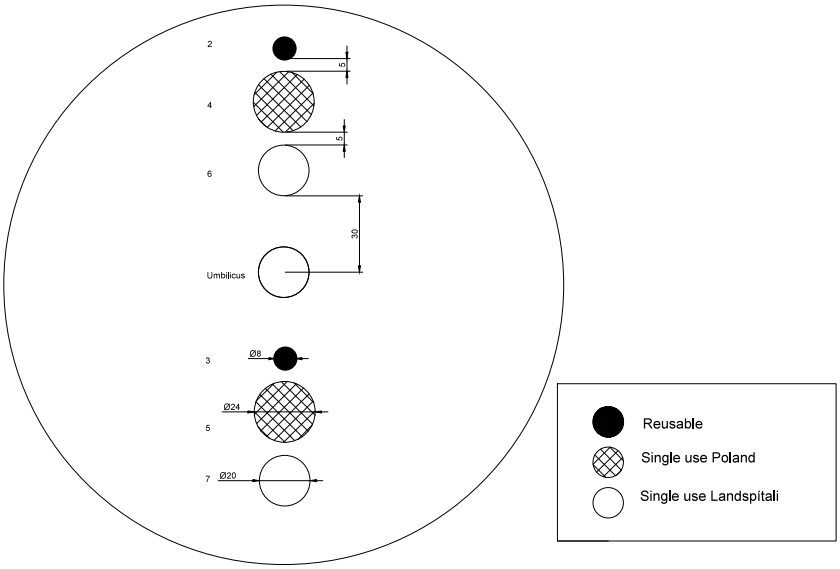

Figure 5. Schematic drawing of the setup. The numbers (mm) indicate contact areas of electrodes and distance between them.

2.2 Frequency analysis of contractions

The data from the measurements were analyzed using MATLAB. It was used to calculate values for the parameters from the poly5 file and the record file. The code used was adapted from previous work in the group(21-23) and can be seen in the appendix.

2.3. Statistical analysis

The Mann Whitney U test is a nonparametric test of the null hypothesis that two samples come from the same population against an alternative hypothesis that one distribution tends to have larger values than the other. The parameters for all contractions for different electrodes were compared using the Mann Whitney U test. Parameters from electrodes of same kind but different location (above vs. below the umbilicus) were also compared with the same test. P-values below 0.05 were considered significant. Statistical analysis and calculations were performed in Excel and the software R. The median, mean and standard deviation of all parameters for all electrodes were calculated and boxplots used to visualize the variance of data.

Results

The five parameters (MPF, PEAK, F10, F50, F95) were calculated for all electrodes. To simplify the text the reusable electrodes are called 1, the single use electrodes from Poland 2 and single use EKG from Landspitali 3. The letter “a” indicates location above the umbilicus and the letter “b” below it (Table 1).

Electrodes		MPF	PEAK	F10	F50	F95
1a	**Median**	0.3329	0.0622	0.0489	0.0907	0.6358
	Mean	0.3991	0.0682	0.0496	0.0935	1.8360
	Standard deviation	0.2160	0.0216	0.0080	0.0219	1.7941
1b	**Median**	0.2827	0.0590	0.0473	0.0861	0.6181
	Mean	0.3205	0.0685	0.0486	0.0939	1.4512
	Standard deviation	0.1383	0.0262	0.0073	0.0270	1.5002
2a	**Median**	0.2960	0.0582	0.0495	0.0840	0.6264
	Mean	0.3328	0.0623	0.0486	0.0918	1.3430
	Standard deviation	0.1644	0.0170	0.0085	0.0254	1.3962
2b	**Median**	0.3222	0.0592	0.0476	0.0880	0.8892
	Mean	0.3533	0.0645	0.0481	0.0900	1.6691
	Standard deviation	0.1575	0.0193	0.0072	0.0244	1.5890
3a	**Median**	0.2964	0.0590	0.0479	0.0908	0.6986
	Mean	0.3031	0.0673	0.0474	0.0913	1.1971
	Standard deviation	0.1256	0.0246	0.0082	0.0244	1.2363
3b	**Median**	0.3520	0.0584	0.0455	0.0804	1.4982
	Mean	0.3881	0.0660	0.0472	0.0893	2.0190
	Standard deviation	0.1760	0.0227	0.0070	0.0281	1.6455

Table 1. Median, mean and variance of data for all electrodes in Hz.

Mann Whitney U test was used to compare all parameters for all electrode types, there was not a significant difference between different electrode types, significant p-values are written in bold (Table 2).

Electrodes	MPF	PEAK	F10	F50	F95
1 vs. 2	0.7571	0.3111	0.6000	0.4050	0.8540
1 vs. 3	0.9554	0.4866	0.1292	0.2704	0.8784
2 vs. 3	0.7256	0.8010	0.8006	0.7783	0.5811

Table 2. P-values from Mann Whitney U tests, comparison of different electrode types.

Mann Whitney U test was also used to compare measurements above and below the umbilicus. There was a significant difference for electrode type 3 (Landspitali EKG) for two parameters; MPF and F95, other comparisons were non-significant (Table 3).

Electrodes	MPF	PEAK	F10	F50	F95
1a vs. 1b	0.0695	0.7703	0.6587	0.8501	0.4916
2a vs. 2b	0.4586	0.5615	0.6300	0.8330	0.2913
3a vs. 3b	**0.0182**	0.9830	0.8007	0.5498	**0.0082**

Table 3. P-values from Mann Whitney U test, comparison of different locations.

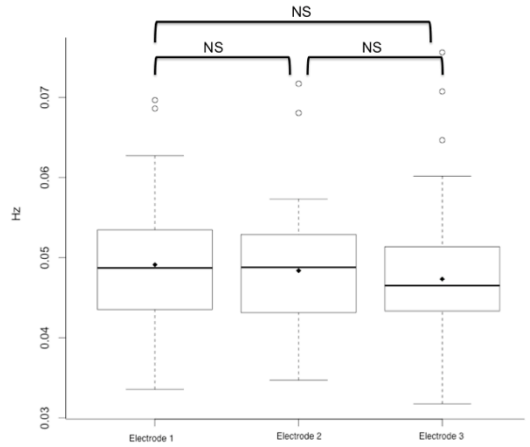

Figure 6. Boxplot showing F10 for different electrodes. There was a non-significant (NS) difference between electrode types. The thick line indicates the median of the data but the dot the mean.

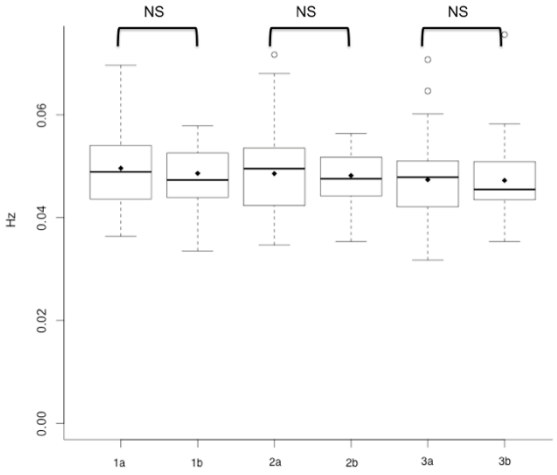

Figure 7. Boxplot showing F10 for different locations. There was a non-significant (NS) difference between locations. The thick line indicates the median of the data but the dot the mean.

The difference for all the parameters obtained for different locations was compared to difference caused by different electrode types (Table 4). The same comparison was calculated for the absolute values of the difference (Table 5).

	MPF	PEAK	F10	F50	F95
1a-1b vs. 1a-2a	0.6463	0.4481	0.9839	0.5146	0.2400
1a-1b vs. 1a-3a	0.3519	0.5559	0.7710	0.7720	0.3079
2a-2b vs. 2a-1a	0.3310	0.7037	0.1685	0.4592	0.3784
2a-2b vs. 2a-3a	**0.0104**	0.6596	0.9693	0.9843	0.0590
3a-3b vs. 3a-1a	0.6396	0.8493	0.1270	0.4783	0.3619
3a-3b vs. 3a-2a	**0.0119**	0.1450	0.2133	0.3520	**0.0073**
1a-1b vs. 1b-2b	**0.0073**	0.5684	0.6387	0.2183	0.0645
1a-1b vs. 1b-3b	**0.0005**	0.5696	0.8967	0.3167	**0.0021**
2a-2b vs. 2b-1b	**0.0011**	**0.0082**	0.1946	0.2530	**0.0034**
2a-2b vs. 2b-3b	0.9526	0.5230	0.8407	0.9430	0.4010
3a-3b vs. 3b-2b	**< 0.001**	0.3534	0.1516	0.4587	**< 0.001**
3a-3b vs. 3b-1b	**< 0.001**	0.8256	0.1293	0.2969	**< 0.001**

Table 4. Differences between location and electrode types compared. The difference caused by different location was in general larger than the difference caused by different electrode types. Table shows p-values.

	MPF	PEAK	F10	F50	F95
|1a-1b| vs. |1a-2a|	**0.0040**	**0.0146**	**< 0.001**	0.0800	**0.0054**
|1a-1b| vs. |1a-3a|	0.1996	**< 0.001**	**< 0.001**	**< 0.001**	0.1933
|2a-2b| vs. |1a-2a|	**< 0.001**	**< 0.001**	**0.0165**	**0.0180**	**0.0428**
|2a-2b| vs. |2a-3a|	**0.0384**	**0.0019**	**0.0209**	**< 0.001**	**< 0.001**
|3a-3b| vs. |3a-2a|	**0.0014**	**0.0010**	**0.0199**	**0.0044**	**< 0.001**
|3a-3b| vs. |1a-3a|	0.5133	**< 0.001**	0.9598	0.9748	0.2334
|1a-1b| vs. |1b-2b|	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**
|1a-1b| vs. |1b-3b|	**0.0374**	**0.0110**	**< 0.001**	**< 0.001**	**0.0550**
|2a-2b| vs. |1b-2b|	**0.0039**	**< 0.001**	**< 0.001**	**< 0.001**	**0.0006**
|2a-2b| vs. |2b-3b|	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**0.0027**
|3a-3b| vs. |3b-2b|	**< 0.001**	**< 0.001**	**< 0.001**	**< 0.001**	**0.0003**
|3a-3b| vs. |1b-3b|	**0.0121**	**< 0.001**	**0.0007**	**0.0004**	0.0593

Table 5. Absolute values for difference between location and electrode types compared. Table shows p-values.

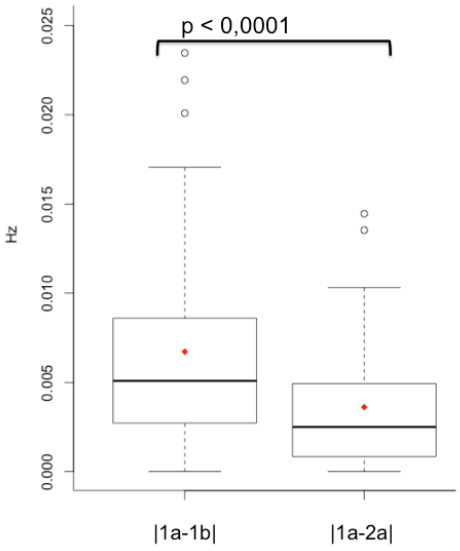

Figure 8. Comparison of difference because of location and because of electrode type for F10 (absolute values). A significant difference was observed. The thick line indicates the median of the data but the dot the mean.

Discussion

There was not a significant difference for any parameter between different electrode types. Based on that information researchers should be able to use which ever type (of those three) that suits their researchers best. This has a practical meaning because different electrode types have different strengths and weaknesses. The single use electrodes are low-cost and easier to apply on the patient while the reusable electrodes are more expensive and require longer preparation time. The reusable electrodes have smaller diameter and are therefore better suited to measure the propagation of the EHG signal.

F10 is the frequency below which the PDS contains 10% of the total energy of the signal. If the electrodes are unequally capable of observing the lowest frequency part of the EHG signal, the biggest variance will most likely be seen in this parameter. Therefore F10 was examined specially (Figures 6-8).

When different locations were compared MPF and F95 for electrode 3 (Landspitali EKG) had significant differences. Thirteen of fifteen values were non-significant. Therefore it can be concluded that location below and above the umbilicus is not of general importance to these measurements.

When we tested if there was a significant difference between variability caused by location and by electrode type p-values were significant in 3 of 16 cases (21.7%) (Table 4). Using absolute values in the calculations increased this ratio dramatically to 86.7% (Table 5). This great increase

shows that the parameter values are sometimes higher above the umbilicus and sometimes below it, in other words, there is no trend for the parameters values to be higher at one place. We therefore assume that one location does not cause the parameters to be higher than the other as could be explained by different skin or fat distribution above and below the umbilicus. These results rather indicate that there is a persistent difference in electrical activity above and below the umbilicus and we can suspect that there are generally major differences in the activity at different places in the uterus. Therefore we conclude that it does not matter if measurements are carried out above or below the umbilicus but it is important to keep in mind that electrodes placed far from each other are not measuring the same electrical activity of the uterus.

Despite not being able to show significant difference between electrode type or location further studies are necessary on the subject. Many factors contribute to the great variance in data and although this research did not show that certain factors matter they cannot be excluded. Future studies with more contractions, more locations and more varied electrode design could either strengthen our results or weaken them.

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Special thanks to my brother Daníel Freyr Jóhannsson and friends Ármann Óskarsson and Jón Atli Jóhannsson for sharing their engineering knowledge with me.

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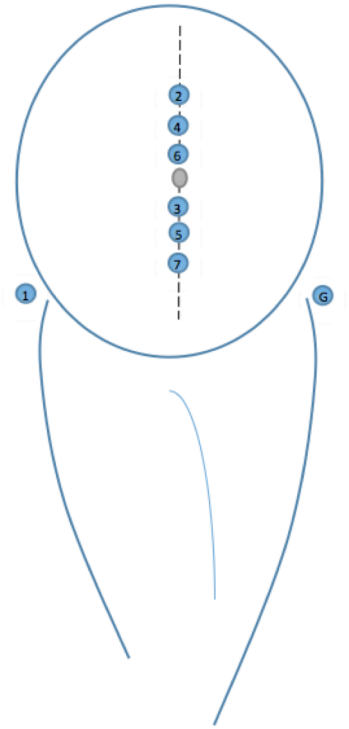
Measurement setup for EHG electrode comparison measurements LSP

March-April 2015. Draft 10.03.215.

Protocol 1. Small electrodes only.



Electrodes.

ISL	Reusable Ag/AgCl (white)
PL	Single use Poland
LSP	Single use Landspítali

Channel list.

GRD	ISL GND	Left hip
Channel 1	ISL0 (ref)	Right hip
Channel 2	ISL1	1
Channel 3	ISL2	2
Channel 4	PL1	3
Channel 5	PL2	4
Channel 6	LSP1	5
Channel 7	LSP2	6

All electrodes will be placed on the centerline of the uterus, a set of three above the umbilicus and three below.

The space above and below the umbilicus to the active surface (gel) of the first electrode should be 3cm.

The space between electrodes should be such that the they do not physically touch and the distance between the active electrode surfaces should be at least 5 mm.

If the electrodes are not circular their longer axis should be perpendicular to the centerline so that they occupy as little space as possible on the centerline.

The configuration should be as similar as possible for all the subjects.

A detailed drawing, photos and measurements of the resulting electrode geometry will be made for at least one subject.

End.

MATLAB codes

```
function TSMICreateVertBipolEHG(signal)

clc
close all

FechSig = 256;

Fch = .033/(FechSig/2);
Fcb = 10/(FechSig/2);
[ah,bh] = butter(4,Fch,'high');
[ab,bb] = butter(4,Fcb,'low');

PrbLength = 10*FechSig;

MatEHG = [];

for CurChan = 1:7
    CurEHG = signal.data{CurChan};

    CurEHG = filtfilt(ah,bh,CurEHG);
    CurEHG = filtfilt(ab,bb,CurEHG);

MatEHG = [MatEHG; CurEHG];

end
MatVert = [[2;4],[4;6],...
            [3;5],[5;7]];


MatBipolVert = [];

for CurVert = 1: size(MatVert,2)
    MatVert(1,CurVert);
    MatVert(2,CurVert);
    size(MatEHG(MatVert(1,CurVert),:));
    BiPol = MatEHG(MatVert(1,CurVert),:) - MatEHG(MatVert(2,CurVert),:);

    BiPol = filtfilt(ah,bh,BiPol);
    BiPol = filtfilt(ab,bb,BiPol);

Long = length(BiPol);
    BiPol(1:PrbLength) = 0;
    BiPol(Long-PrbLength-1:Long) = 0;
MatBipolVert = [MatBipolVert; BiPol];
end


save(' "filename"_Bipol.mat','MatBipolVert')



MatRHVert = [[1;1],[2;1],[3;1],...
            [4;1],[5;1],[6;1],[7;1]];
```

```
  MatRefhipVert = [];

  for CurRHVert = 1: size(MatRHVert,2)
      MatRHVert(1,CurRHVert);
      MatRHVert(2,CurRHVert);
      size(MatEHG(MatRHVert(1,CurRHVert),:));
      Refhip          =          MatEHG(MatRHVert(1,CurRHVert),:)          -
MatEHG(MatRHVert(2,CurRHVert),:);

      Refhip = filtfilt(ah,bh,Refhip);
      Refhip = filtfilt(ab,bb,Refhip);


      LongRH = length(Refhip);
      Refhip(1:PrbLength) = 0;
      Refhip(LongRH-PrbLength-1:LongRH) = 0;

  MatRefhipVert = [MatRefhipVert; Refhip];
  end

  save('"filename"_Refhip.mat','MatRefhipVert')


  SegNewCT.m

  close all
  clear all
  clc
  load "filename"_Monopol.mat
  load "filename"_Bipol.mat
  load "filename"_Refhip.mat
  CT=[];
  CTbipol=[];
  CThip=[];

  MatEHG=MatEHG;
  MatBipolVert=MatBipolVert;
  MatRefhipVert=MatRefhipVert;

  S1=MatEHG(3,:);
  Fech = 256;
  N = length(S1);
  VectT = [0:N-1]/(Fech*60);


  S2=MatBipolVert(3,:);
  Fech = 256;
  N = length(S2);
  VectT = [0:N-1]/(Fech*60);

  S3=MatRefhipVert(3,:);
  Fech = 256;
  N = length(S3);
  VectT = [0:N-1]/(Fech*60);

  subplot(3,1,1)
  plot(VectT,S1),axis tight
```

```
hold on
subplot(3,1,2)
plot(VectT,S3),axis tight
hold on
subplot(3,1,3)
plot(VectT,S2),axis tight
hold on

pause
[x,y] = ginput(1);
xDeb = fix(x*Fech*60);
yDeb = fix(y);
plot(x, y, 'g*')

 [x1,y1] = ginput(1);
xFin = fix(x1*Fech*60);
yFin = fix(y1);
plot(x1, yFin, 'g*')

for i=1:7
Si=MatEHG(i,:);
s=Si(xDeb:xFin);
size(s);
CT=[CT; s];
figure(2)
plot((0:length(s)-1)/(60*256),s);
end
save  ”filename”_CTMono5.mat CT;

for i=1:7
Si=MatRefhipVert(i,:);
s=Si(xDeb:xFin);
size(s);
CThip=[CThip; s];
figure(3)
plot((0:length(s)-1)/(60*256),s);
end
save  ”filename”_CTHipref5.mat CThip;

for i=1:4
Si=MatBipolVert(i,:);
s=Si(xDeb:xFin);
size(s);
CTbipol=[CTbipol; s];
figure(4)
plot((0:length(s)-1)/(60*256),s);
end
save  ”filename”_CTBipol5.mat CTbipol;
```

VÍSINDASIÐANEFND

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Hringbraut
101 Reykjavík

Reykjavík 24. febrúar 2015
Tilv.: VSNb2015020009/03.11

Efni: Varðar: 15-032-afg Áhrif rafskautstegundar á legrafritsmerki.

Umsókn þinni til Vísindasiðanefndar hefur verið gefið númerið **VSN-15-032**. Við förum vinsamlegast fram á að það númer verði notað vegna þessarar umsóknar.

Á fundi sínum 24.02.2015 fjallaði Vísindasiðanefnd um umsókn þína. Meðrannsakendur þínir eru: Ásgeir Alexandersson, Brynjar Karlsson og Marta Sigrún Jóhannsdóttir.

Eftir að hafa farið vandlega yfir umsókn þína og innsend gögn gerir Vísindasiðanefnd ekki athugasemdir við framkvæmd rannsóknarinnar. Rannsóknaráætlunin er endanlega samþykkt.

Vísindasiðanefnd vekur sérstaka athygli á að ábyrgðarmaður rannsóknarinnar ber ábyrgð á að sótt sé um viðeigandi leyfi fyrir rannsókninni hjá þeim stofnunum sem við á. Óheimilt er að hefja framkvæmd rannsóknarinnar fyrr en þau liggja fyrir. Afrit leyfa/samstarfsyfirlýsinga þurfa að berast nefndinni. Áréttað er að allar fyrirhugaðar breytingar á þegar samþykktri rannsóknaráætlun þurfa að koma inn til nefndarinnar til umfjöllunar. Jafnframt ber ábyrgðarmanni að sækja um breytingar til þeirra stofnanna, sem veitt hafa leyfi vegna framkvæmdar rannsóknarinnar eða öflunar gagna, um framangreint, ef við á.

Vísindasiðanefnd bendir rannsakendum vinsamlegast á að birta VSN tilvísunarnúmer rannsóknarinnar þar sem vitnað er í leyfi nefndarinnar í birtum greinum um rannsóknina. Minnt er á að tilkynna rannsóknarlok til nefndarinnar.

Með kveðju og ósk um gott rannsóknargengi,
f.h. Vísindasiðanefndar,

Kristján Erlendsson, læknir, formaður

LANDSPÍTALI
HÁSKÓLASJÚKRAHÚS

Þóra Steingrímsdóttir, prófessor
kvennadeild LSH

Reykjavík, 10. febrúar 2015
ÓB/eí Tilv.16

Efni: Áhrif rafskautstegundar á legrafritsmerki

Ágæta Þóra.

Vísað er til erindis þíns til framkvæmdastjóra lækninga 6. febrúar sl. þar sem óskað er heimildar til að gera ofangreinda rannsókn á Landspítala. Um er að ræða viðauka við rannsóknina Legrafrit I. Þróun mæliaðferða og er þetta nemaverkefni 3. árs nema í læknisfræði. Fram kom að þú ert ábyrgðarmaður rannsóknarinnar og samstarfsmenn eru Marta Sigrún Jóhannsdóttir, læknanemi við Háskóla Íslands, Ásgeir Alexandersson, leiðbeinandi og Brynjar Karlsson, prófessor, báðir í verkfræðideild Háskólans í Reykjavík.

Hér með er veitt heimild til að ofangreind rannsókn fari fram á LSH og jafnframt er veittur aðgangur að sjúkraskrám sem tengjast kunna rannsókninni. Leyfi þetta er háð því að fyrir liggi samþykki Vísindasiðanefndar og mun aðgangur að sjúkraskrám verða opnaður þegar sú heimild liggur fyrir.

Með kveðju og ósk um gott rannsóknargengi,

Ólafur Baldursson,
framkvæmdastjóri lækninga

Afrit:

Kristján Erlendsson, formaður Vísindasiðanefndar
Jón Hilmar Friðriksson,framkvæmdastjóri
Magnús Gottfreðsson, yfirlæknir vísindadeildar
Ingibjörg Richter, kerfisfræðingur

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