Kandidat speciale

AALBORG UNIVERSITET

School of Medicine and Health

Seismocardiography as method for studying acute alcohol related hemodynamic changes

With mechanical changes as a focus

4. Semester, Klinisk Videnskab og Teknologi
Group: 20gr10518

Writer
Lasse W. Ibsen

Counselor:
Samuel Schmidt

June 2, 2020

Contents

1 Acstract

Introduction: Seismography has a long history, however advancements in todays technology have meant we are now able to record and analysis more data and, in more detail than ever before. To this end, this study aimed to discover if Seismocardiography be used to see changes in hemodynamics while under the influence of alcohol. **Method:**The method used to investigate and collect data on this area of study will involve a pre trial and trial stage. The pre trial focused on creating awareness about the trial, sourcing participants and giving them information about what they will experience and instructions on what they can do to prepare prior to the study. The main trial incorporated a few different elements, such as taking personal details (height, sex, etc) followed by participants consuming 0.5g of alcohol per 1kg of weight. At regular intervals the participants will be required to rest and the Seismocardiograph will be used to measure their heart rate. This was repeated in a total of three separate sessions. **Results:** Most of the findings pointed in the direction of previous studies, a part from the PEP value that fell unexpectedly, same for the QT interval. **Conclusion:** The SCG results all correlate very well with what was expected from literature, with the AO amplitude showing a decrease after acute ingestion of alcohol, undetectable with an ECG only

2 Introduktion

Seismocardioprahy is the descriptive science of the vibrations caused by the heart.

2.1 History

In 1877, the first recordings of cardiac vibrations, measured by resting on a surface that could detect vibrations, was done by J. W. Gordon[1]. Gordon found a rhythmic pattern, synchronous with the pulse and that during systole the measurements would show a vigorous movement and during diastole the movement would be slower and return to the starting point[1].
In 1905 a study was done, recording the bloods impact on the moment of the human body. A "swinging table" was used and it was suggested that the movements recorded were related to cardiac output[2]. Further studies were conducted in 1913 and 1922 with the latter study showing cardiac movement, without the interference of normal respiratory cycles. Increase in amplitude was shown after exercise or medical intervention in the form of nitroglycerine[2]. In 1939 the term Ballistocardiogram (BCG) was used to describe the motions captured by recording vibrations done by the whole body in rest, the method was calibrated using both living and dead bodies to remove as much error as possible. Multiple studies were done on humans of varying body size and composition, with some of the measured vibrations held up against an electrocardiogram for comparison and correlation. The researchers conclude that a ballistocardiogram is an efficient way to measure cardiac changes over time for a single person especially[2].
Studies done up to this point were only done on healthy humans but in 1943[3], 1952[4] and 1953[5] studies were conducted on people with known cardiac disease and in 1961 Russian researcher Bozhenko changed approach from measuring the vibrations from the whole body to measure directly on the chest wall, the new approach was named seismocardiography (SCG). [6]
From 1955 to 1985 over 330 publications about BCG were conducted, with a peak in the early 1960's[7] but even though the studies, already back then, showed a good potential in BCG and later SCG, the methods would not be used in clinical studies until 30 years later in 1991 by Salerno and Zanetti. The pair proved a significant difference in SCG recorded on patients during an ischemic episode, compared to recordings done on five control individuals.[8]
Between 1990 and 2010 almost no studies with BCG or SCG were done, for two main reasons. Firstly echocardiography and ultrasound techniques were refined and widely spread as a new techniques for non-invasive cardiac and hemodynamic diagnostic and therefore pushing the need for, and research in BCG and SCG in the background. Secondly the electronic components needed for BCG and especially SCG were not up to a reasonable standard in quality, size and cost yet.[7]
In recent years the technological advancements has simplified the tools needed for measurement but also the assessment of BCG and SCG signals. These advancements has opened up new perspectives and viable situations for clinical use.[9]
Since 2010 multiple studies have been conducted to understand and find clinical use for SCG (especially) and similarly with the technical approach. Three-Dimensional Apex-Seismocardiography from 2014[10], Challenges in using Seismocardiography for Blood Pressure Monitoring from 2017[11], Definition of Fiducial Points in the Normal Seismocardiogram from 2018[12] and Visualization of the Multichannel Seismocardiogram 2019[13] are all good examples of these newer studies done with Seismocardigraphy as a focus.

2.2 Understanding and using Seismocardiography

Seismocardiography has from early days been linked with other ways of measuring the heart like the ECG and by measuring the vibrations caused by the heart, especially mitral- and aorta valve opening and closing are clear to see. Same goes for the positiv and negative acceleration monitored on SCG that is not present in a ECG[14]
To understand exactly how to determent what parts of the SCG is linked to the different parts of the heart cycle, researchers have done simultaneous measurements like ECG or Ultrasound and determined where predetermined fiducial points would be found[12]. As seen in fig.: 1, 8 key points exists in a seismocardiogram: Atrial systole (AS), peak atrial infow (PAI), mitral valve closure (MC), aortic valve opening (AO), peak systolic inflow (PSI), aortic valve closing (AC), mitral valve opening (MO), early ventricular filling (EVF)[12]

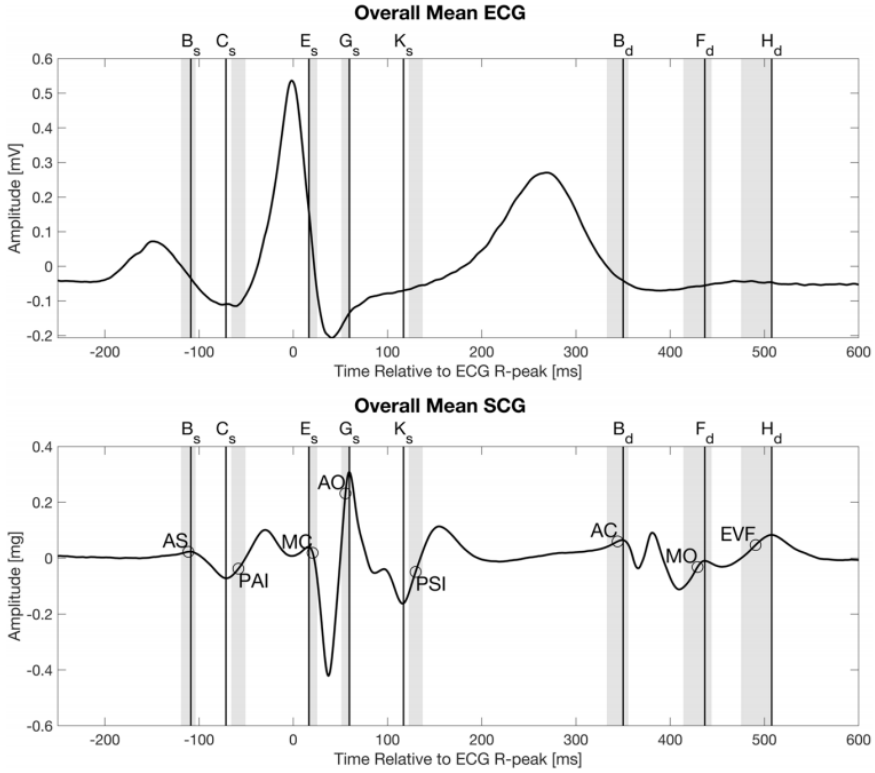

Figure 1: Mean Fiducial points found comparing SCG and Ultrasound findings[12]

Measuring a seismocardiogram has been tried in different ways, but most studies have either used- or come to the conclusion that, patients in rest and in a supine position is superior[9]. Studies with different stressors have been done, but the actual live measuring of SCG has happened as soon as the subject could rest[14]. A study from 2011 did measure SCG during daily activities, with the person wearing a vest with the necessary equipment sown into the fabric. The study could find clean, noise free data in amongst the noise caused by physical movement, it still took the person to naturally sit still for 30 seconds or more [15].
To further strengthen the understanding of a SCG, a study from 2019 did a multi-channel seismocardiogram, allowing for a 3D visualisation of the vibrations caused by

the heart, conducted in a supine and rested position. [13].

3 Problem analysis

3.1 Problem analysis

As seen in many studies done in the past, BCG and SCG has been held up against ECG data recorded simultaneously as seen in [2] [3] [4] [5] [6]. Newer studies often use the same approach [16], where other measuring other than SCG and ECG is done simultaneously, but the ECG is always there for comparison. For a study in alcohols effect on the heart, seen through the mechanical view of SCG, it would make sense to hold the collected data up against data collected with ECG.

Through out history alcohols on the heart has been studied through especially ECG. In 1996 a study was conducted on 10 subjects who all drank a measured amount of alcohol, with 8 subjects as a control group. A set of baseline- and follow up measurements were done at BAC 0 g/dl, 0.25 g/dl and 0.75 g/dl. Signal-averaged P waves and QRS complexes were compared by 2 investigators by superimposing the computer-generated signal-averaged P waves and QRS complexes. 90% of subjects were found to have a significantly prolonged P wave and 100% had a significantly prolonged QRS complex. P waves and QRS complexes were found to be longer in the control group after ingesting fluids, but not significantly from the baseline. [17]
A study from 2005, had a similar focus on the P wave after acute intake of alcohol. The subject ingested 1g/kg of alcohol over a 1 hour period, rested for 1 hour and then another set of recordings were done. Pmin and Pmax were annotated and Pdelta was calculated. The study found a significantly prolonged Pdelta after the ingestion of alcohol, but not during control. [18] A study from 2007 included 84 patients, hospitalised with assumed acute ethanol intoxication. A total of 32 patients had ECG recordings conducted on them, both on admittance and at discharge, as well as 27 control patients, who were not ethanol intoxicated. They found that P wave and QTc intervals were prolonged compared with sober subjects. P wave, PR, QRS and QTc intervals were longer when the subjects had high blood ethanol levels at admission than at discharge. [19] A systematic review from 2017, including the above mentioned studies, with a total of 141 patients included found 90 (63.8%) patients had P-wave prolongation, 80 (56%) patients had QTc prolongation, 19 (13.5%) patients developed T-wave abnormalities, 10 (7%) patients had QRS complex prolongation, 3 (2.12%)patients developed ST-segment depressions [20]

All these studies all found changes in the ECG data obtained, but have no data on the mechanical changes in the heart while under the influence of alcohol. Early studies done on dogs, showed a drop in ejection fraction, by as much as 10%. [21] But with the limited information ECG data can give, these things are missed.
A study from 1978 monitored 17 patients, after heavy drinking and presenting with arrhythmia. Examination of the patients gave no reason to suspect heart related disease to be the cause of the arrhythmia and 16 of the patients were fully normal after resolution of the alcohol related arrhythmia. Studying the ECG gave some further insight into what effects alcohol has on the hemodynamics of the heart. Two patients had a broad P-wave, two patients had small T wave abnormalities and many had ST-T abnormalities and QT prolongation, but the tracings returned to normal within 48 hours. By combining ECG and SCG data, PEP and LVET timings were annotated and calculated. The mean PEP was longer and the mean LVET was shorter in patients and after adjusting for pulse, the adjusted mean PEP for patients (136 -+ 3 msec.), age matched control

(116 -+ 3 msec., P <0.001) and adjusted mean LVET for patients (383 -+ 7 msec.), age matched control (407 -+ 3 msec., P <0.005) [22]
As the study from 1978 showed, more data and understanding about the effects of alcohol intoxication can be found using equipment apart from the ECG. To have a further and more precise look at the heart Doppler echocardiography can be used and a study from 2008 used Doppler echocardiography as well as ECG to see alcohols effect on the heart. With the Doppler echocardiography technology it is possible to study the mechanical movements of the heart and gather data on stroke volume and cardiac output. The study found a slight drop in systolic pressure, stroke volume and cardiac output in the initial intake of alcohol, but a correction back to normal after further alcohol intake. [23]

Doppler echocardiography in the form of M-mode, pulse-wave or tissue imaging is not as readily available as ECG, takes specific training and a constant live setting to gather data [24]. Therefore, Doppler echocardiography and the data possible to gather was witnessed in the study from 1978 [22], will often be missed out unless cardiac failure is expected. A case study from 1991, based on a cardiac patient with a lowered ejection fraction amongst other things, found a correlation between the AO fiducial point amplitude (*named "RE" in original paper*) measured on a SCG and the treatment of the patient. Before medical treatment, while the patient has a low ejection fraction, the AO amplitude was small, even smaller than the MC fiducial point. As the medication helped the underlying cardiac problem, the patient regained a normal ejection fraction and the AO amplitude regained its height. [8] As the above mentioned studies show, alcohol alters the hemodynamics of the heart seen through ECG and ECG-SCG combined. The mechanical changes, seen through amplitude changes are missed because SCG is used in combination with ECG and not for its stand alone values like AO amplitude and LVET. When studying alcohols effect on the hemodynamics its stand to reason that the SCG data is collected and used, so the problem statement is:

3.2 Problem statement

Can Seismocardiography be used to see changes in hemodynamics while under the influence of alcohol

4 Literature search

This section presents the search string used to find scientific articles selected in the background and problem analysis.
A literature search is based on a coverage of literature within a selected topic. A loose structure can be used in the search, called narrative literature search, where the purpose is to gain an overview of the topic and become familiar with relevant keywords. A more structured search, know as a systematic literature search is based on a predefined structure and purpose. Both aim to ensure knowledge coverage within a given problem area, as well as to document an existing knowledge gap. [25].
Through narrative literature searches keywords are found and structured for the systematic literature search
In- and exclusion criteria is set for what articles will be used and what articles fall outside the score op the study.
Relevant databases are used as well as needed boolean operators
Found articles are screened through title and abstract to be sorted using the In- and exclusion criteria.
Included articles are then read fully through. [25]

4.1 Narrative literature search

Given very no articles were found focusing on alcohols effect on the heart and Seismocardiography, a lot of the articles used in this study is found through narrative literature searches. Stand alone keywords like *seismocardiografi*, *balistocardiography*, *Alcohol*, *Ethanol*, *Holiday heart syndrom* and *Hemodynamics* were used. From articles found, chain searching was used to gather information about other studies done about the subject.

4.2 Choice in databases

The choice of databases was of great importance to ensure the coverage of the problem area as a whole. Here it was of great importance to consider the types of articles accepted by the various databases, who their target group was and whether there was evidence of underlying political interests. [25]
PubMed, Embase, Cochrane and Google Scholar were chosen as they are the 4 biggest search engines regarding medical studies.

4.3 Systematic literature search

The systematic literature search was build as a block search, using keywords. The keywords are combined with Boolean operators and where possible search engine specific tools were used eg. MeSH words. [26]

Table 1: Systematic literature search. Truncation is indicated by *

Medical change		**Recording method**
Alcohol OR Ethanol	AND	Seismocardio*

In- and exclusion criteria In- and exclusion criteria can be very strict to allow for a homogeneous selection process from a large amound of articles. During this search, very few articles were available from the keyword Seismocardiography alone, and with Alcohol or Ethanol even fewer. The In- and exclusion criteria will reflect that, and becomes very similar to the block search.

Table 2: In- and exclusion criteria

Inclusion	Exclusion
Seismocardiography and either Ethanol or Alcohol	All other studies

4.4 Sorting articles

After searching on PubMed, Embase, Cochrane no articles were found. Using Google scholar 3 articles were found, but non of them fit the inclusion criteria. A flow chart over the search can be seen on figure: 2

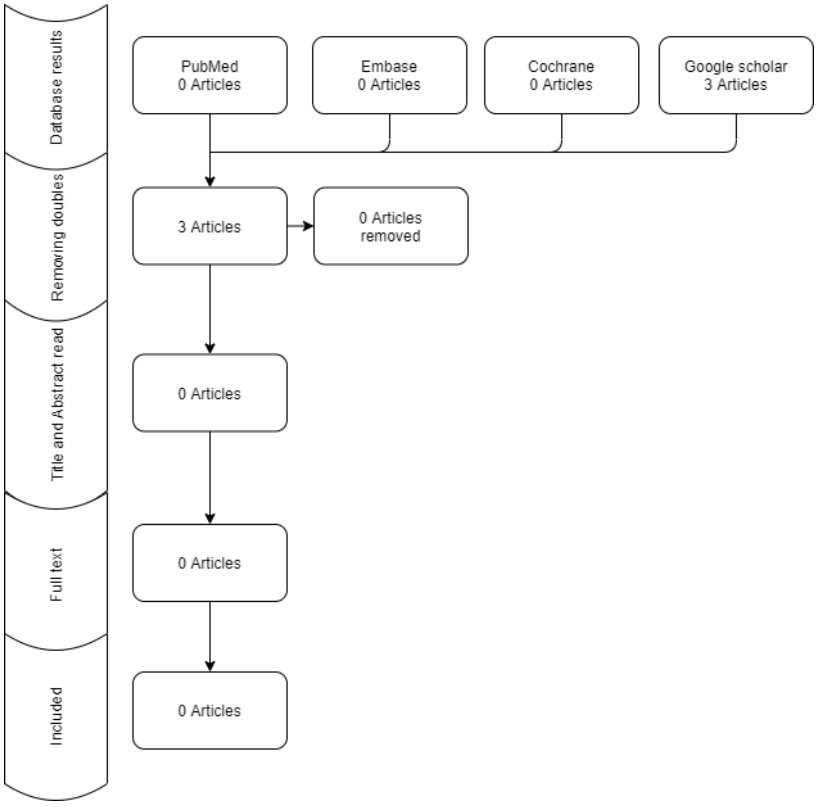

Figure 2: Flowchart over the systematic literature search

5 Hypothesis and expected outcome

The problem statement is based on SCG data so will the main hypothesis and expected outcome be. As the effect of alcohol seen in ECG data is better studied, the secondary hypothesis and expected outcome will be based on ECG data.

Main hypothesis: Acute ingestion as alcohol will be visible in the gathered SCG data, not only in the timings of intervals but also in amplitude of the AO fiducial point.

Secondary hypothesis: Acute ingestion as alcohol will be visible in the gathered ECG data.

From the main hypothesis, the following expected outcomes:

- mean PEP time will be longer after ingestion of alcohol [22]
- mean LVET time will be shorter after ingestion of alcohol [22]
- EF will drop [21] and it will show by the mean AO amplitude getting shorter [8]

From the secondary hypothesis, the following expected outcomes:

- mean P wave time will be longer after ingestion of alcohol [17] [18] [19] [20]
- mean QRS time will be longer after ingestion of alcohol [17] [18] [19] [20]
- mean PR interval time will be longer after ingestion of alcohol [19] [20]
- mean QT interval time will be longer after ingestion of alcohol [19] [20]
- mean Systole, Diastole and Heart rate will rise [23]

Given that the equipment and expertise needed to scan for unknown heart conditions, the verbal confirmation from each subject will be used as validation.
EF, T wave abnormalities, ST segment depression are not within the reach of this study, non of these will be concluded on.

6 Method

To answer the research question, through expected outcome, the following protocol was followed. On figure 3 is an overall flowchart, with both pretrial and trial days. After that a run down of the trial step by step. The protocol is based on National Videnskabsetisk komité's guidlines on clinical trials [27] and literature on previous clinical trials, all with alcohols effect on the heart as focus.
By predetermining expected outcomes, the protocol will reflect the data needed to be generated, and ensures that no subject is taking part in unneeded parts of a clinical trial. In- and Exclusion criteria were also carefully set for the same reason [28]. To ensure the lab safety was up to the expected standard, the guidelines from Webster er al. were followed. [29]
The reliability of both the Seismocardiography equipment and reliability has been proven in previous studies [30], so in this study ECG is used as a reference. As explained in detail in the problem analysis, certain changes in ECG data has been found in other studies on the effect of alcohol on the heart. Some of the expected outcome will be based on ECG findings, to help validate the findings done through collected SCG data. The Pre-Ejection Period (PEP) is based of synchronised ECG- and SCG data. As for the mechanical information, Left ventricular ejection time and Amplitude of the AO fiducial point especially, only SCG data will be used.
The software used in this project were LabScribe 3 for all data recording, data were handled, annotated and plotted with MATLAB R2018b and the statistical tests were done in SPSS 25. SCG data were recorded at 2000 samples per second, following the rule of Nyquists about sample rate [31].
The hardware used in the clinical trial was an iWorx IX-ECG12 [32], an iWorx RA 834 [33] (both: iWork system Inc., USA, New Hampshire, Dover) and a Seismocardiography model 1521 [12] (Silicon Designs Inc, Kirkland, USA). Both hardware and software were on loan from Aalborg Universitet. As for the placement of the SCG recording device, studies have shown that the optimal placement is on the inferior part of sternum, between the (sternum)Body and the Xiphoid process. [34]

6.1 Risks and side effects

During the trial, there is a slight chance of skin irritation or small skin tares from the preparation of the skin and the use of tape and sticky ECG electrodes directly on the skin. To make sure the chance for any skin damage would be as little as possible, special double sided wig tape, made for skin contact was used as well as ECG electrodes used on cardiac hospital settings [35].
During the trial, multiple items of electrical equipment are to be used and the subjects will be directly connected via both ECG and SCG measurements. The subject's personal health is of the uppermost importance and the guideline for correct and safe procedures from John G. Websters book *Medical Instrumentation* [29] will be followed. No modifications were done to either the iWorx IX-ECG12[32], the iWorx RA 834[33] or to the SCG model 1521 [12] (Silicon Designs Inc, Kirkland, USA).

Given alcohol is an intoxicant with multiple effects on the body, and the experiment will be set in a non-hospital setting, extra care is given to ensure no harm will be done to the subjects health. To ensure a balanced alcohol intake, no matter subject size, alcohol was dosed in grams of alcohol per kilogram body mass (g/kg) and previous studies was used as a guideline for dosage. Multiple studies used a dosing of 1g alcohol per 1kg body mass (1g/kg) drunk over 1 hour, a large acute amount of alcohol intake. Given no immediate medical assistance would be present as backup, the dosage was halved to 0,5g

of alcohol per 1kg of body mass (0,5g/kg), the amount of dilutant was set to 1000ml, doubling the dilutant used in other studies. As a last precaution, the total amount of alcohol and dilutant will be served in 4 portions, one for every 15 minutes to ensure a ingestion as evenly over the hour as possible.
All subjects were advised to stop the trial if they started feeling any adverse effects. Plenty of water was also made available for subjects to drink at the end of the trial.

6.2 Ethics

Before any trial involving consequences for any living beings, ethics has to be thought through and evaluated. The Committee Act states that by law, any clinical trials conducted in Denmark must to be declared to the National Science Ethics Committee (National Videnskabsetisk Komité) [36]. The National Science Ethics Committee is subdivided into 5 geographical regions, and the local subsection of the the National Science Ethics Committee, evaluates any request for clinical trials done on humans. The clinical trial is not permitted to start until the full grant is given. [37]
Examples of what needs approval could be research on human biological bio material, research on new methods of care and treatment and research and development of new drugs. Furthermore, approval is also needed by the Science Ethics Committee before conducting research and development of new medical devices or when researching for new/altered use of medical devices, other than the technology originally approved for. [37]
During this project, the Danish government instituted a COVID-19 lockdown baring any subjects for the clinical trial to be sourced for direct contact, even amongst university study partners. The clinical trial was done as a private arrangement with my partner (from here mentioned as STNM), and was therefore not declared to the Science Ethics Committee.

The Helsinki Declaration [38] aims to protect subjects and sets the framework for the necessary ethical considerations that must be assessed both before, during and after research conducted on humans. Test subjects rights during research and clinical trials are essential and first priority no matter the scale of the trial. Clinical trials on humans are often necessary to gain valuable knowledge about disease and the medication/surgery needed. By following the Helsinki Declaration, researchers can assure subjects rights are being upheld and protected [38].
Before agreeing to enter the clinical trial, subjects were informed both verbally and through an initial recruitment letter, about the trial and their ethical rights. Later on, before the trial, a further clinical trial information letter gave a full picture of the clinical trial and what would happen during trial days. By using this approach, and allowing subjects to exit the clinical trial at any point, it is assured the guidelines in the Helsinki Declaration are followed [38].
During this clinical trial, equipment will have to be in skin contact with the torso of the subject. This would leave the subject with a mostly if not fully undressed torso during ECG and SCG measuring. All subjects were made aware of this in the recruitment letter. Furthermore, no data was commented on, assuring subjects did not receive unnecessary or false conclusions based the their recorded data. It was chosen deliberately not to comment on the data based on the lack of diagnostic skills of the tests. The subject was informed in advance that an assessment of their data could not be given.
Because of the COVID-19 lockdown, both researcher and STNM were used as testers and subject. Researcher and STNM were trained in measuring blood pressure, setting up and hooking up ECG and SCG equipment and the use of LabScribe3 before the start of the clinical trial.

Personal information
To ensure that all personal information was kept in accordance with Databeskyttelsesloven [39], each subject was given a unique ID number so file names containing data could not be linked to anyone with out they ID-key. The ID number was assigned as the subject gave signed consent to be a part of the clinical trial and pseudonymization was used for all demographic and recorded data as it was stored with the ID number only. No data was ever transferred over the internet or physically to another person as it was stored and used on the same computer.

6.3 In- and exclusion criteria

Through literature and previous studies, the following inclusion and exclusion criteria were used, to insure both the safety of subjects during the clinical trial and to insure the validation of the results. The Inclusion and exclusion criteria can be seen in the table below. The In- and exclusion criteria can be seen in tabel 3.

Table 3: In- and exclusion criteria

Inclusion criteria	Exclusion criteria
- Over the age of 18 - Healthy	- Known heart disease. - Known disease relating to the heart (eg. COPD or circulatory disorders). - Raised daily intake of alcohol (>36g alcohol pr. day). - Known disease related to alcohol intake. - Any drug use that effects the heart function (eg. Beta blockers / beta-adrenergic blocking agents). - Any drug use that effects the central nervous system (eg. morphine and products containing morphine). - Any illegal drug use. - Tremor. - Pregnancy.

The first 7 exclusion criteria are all related to the function of the heart, and medication/disease that can alter the hearts output and mask the effect alcohol will have. Given that SCG records the mechanical movement of the chest wall, tremor would distort or potentially invalidate recorded data. Pregnant women are automatically excluded as of the EU guidelines for clinical trials, stating no pregnant women should enter clinical trials not aimed at studying pregnant women. [40]

6.4 Clinical trial protocol

Initial clinical trial information and written consent were recorded days in advance of first trial day, to allow for the subject to fulfil the asked requirements. It included the following steps:

- Information about the clinical trial is given verbally and the subject has time to ask any questions regarding the clinical trial and the project as a whole.
- The In- and exclusion criteria are explained verbally and the subject agrees with fitting the framework.

- Written consent is given and the subjects ID number is recorded.

On the day of the first trial a full list of demographic data was recorded, on trial day 2, 3 only the subjects' weight was recorded.:

- Sex.
- Age.
- Weight.
- Smoking habits.
- Drinking habits.

Smoking habits were recorded as Light: <10 cigarettes a day. Moderate: 11-20 cigarettes a day. Heavy: >20 cigarettes a day.
Drinking habits were based on the guidelines given by Sundhedsstyrelsen, Light: Men < 14 units a week, Female: < 7 units a week. Moderate: Men 14-21 units a week, Female: 7-14 units a week. Heavy: Men >21 units a week, Female: >14 units a week. [41]

Each of the three clinical trial days including alcohol were all done in the exact same way, following a predetermined protocol. Figure 3 shows a flowchart of 1 trial day, with the initial setup, and the looping of data recording after 30-, 60-. and 90 minutes post end of alcohol intake.

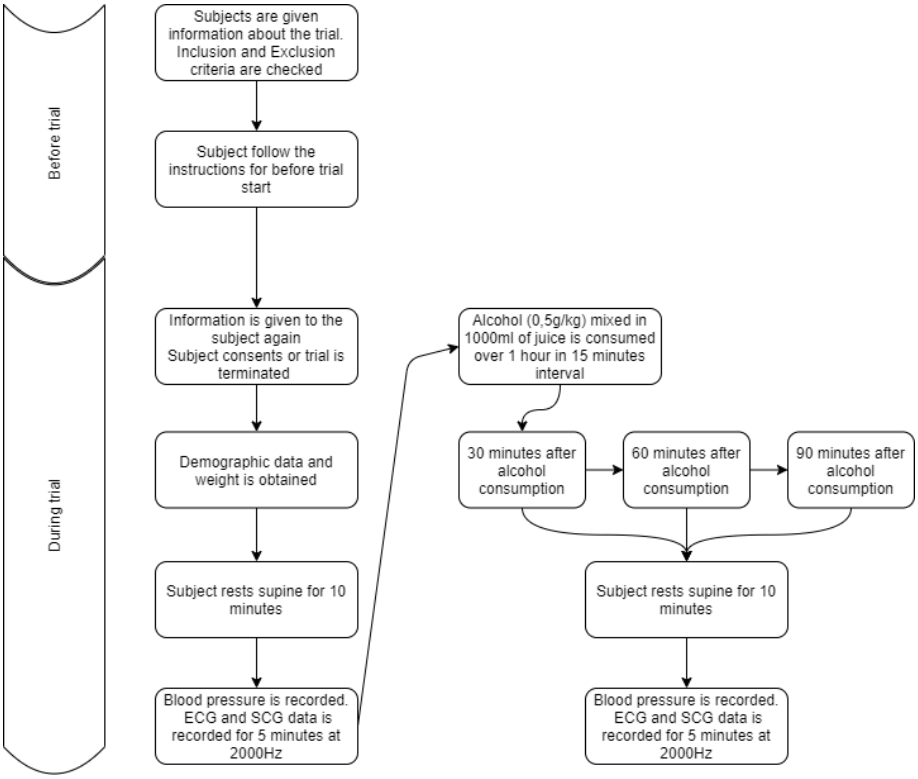

Figure 3: Protocol flowchart

List of materials needed during the clinical trial:

- Seismocardiography recording device (SiliconDesigns Model 1521) [12].
- 5-lead ECG wires. [42]
- H91TSG ECG Electrodes. [35]
- iWorx IX-ECG12. [32]
- iWorx RA 834. [33]
- Double sided tape.
- Computer with LabScribe. [43]
- Razor and alcohol wipes to ready the skin if necessary.
- Weighing scale.
- Blood pressure monitor

The placement of the ECG electrodes and the SCG recording equipment were done as seen in figure 4.

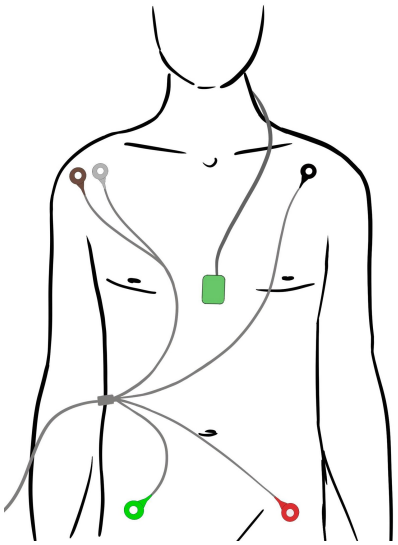

Figure 4: Guideline to the placement of ECG electrodes and the SCG recording equipment

6.5 Trial including alcohol:

The following list is a detailed protocol over the clinical trial. Including the initial steps taking by each subject and each part of the clinical trial

Before trial start:

- Subject will drink no alcohol 72 hours before trial start [18]
- Light breakfast. [17]
- Fasting for 4 hours before trial start. [17]
- no smoking on the day, before trial is over. [17]

Trial start:

- Demography data is collected. [18]
- Subject is weighed. [18]
- 5-lead ECG connected and checked for noise.
- SCG positioned,taped to the chest with double sided tape and checked for noise.
- Subject is resting supine for 10 minutes. [18]

Baseline recording:

- Baseline blood pressure is recorded.
- Baseline ECG and SCG data recorded for 5 minute at 2000Hz. [17]

Alcohol consumption: *section:* [18]

- Alcohol (0,5g/kg) is mixed with 1000ml juice (total 1030-1040ml).
- The alcohol and the mixer is drunk over 1 hour.

Data recording 2: *section:* [44]

- Starts 20 after Alcohol consumption is ended.
- Subject is resting supine for 10 minutes.
- Data is recorded as done during baseline recording.

Data recording 3: *section:* [44]

- Starts 50 after Alcohol consumption is ended.
- Subject is resting supine for 10 minutes.
- Data is recorded as done during baseline recording.

Data recording 4: *section:* [44]

- Starts 1 hour and 20 after Alcohol consumption is ended.
- Subject is resting supine for 10 minutes.
- Data is recorded as done during baseline recording.

Trial end: Subject is given more non alcoholic fluids if needed.

6.6 Control:

The following list is a detailed protocol over the control part of the trial. Including the initial steps taking by each subject and each part of the control

before:

- Subject will drink no alcohol 72 hours before trial start [18]
- Light breakfast. [17]
- Fasting for 4 hours before trial start. [17]
- no smoking on the day, before trial is over. [17]

Trial start:

- Demography data is collected. (If not already done) [18]
- Subject is resting supine for 10 minutes. [18]

Baseline recording:

- Baseline blood pressure is recorded.
- 5-lead ECG connected and checked for noise.
- SCG positioned,taped to the chest with double sided tape and checked for noise.
- Baseline ECG and SCG data recorded for 1 minute at 2000Hz. [17]

Juice consumption: *section:* [18]

- 1000ml juice is drunk over 1 hour.

Data recording 3: *section:* [17]

- Starts 50 after juice consumption is ended.
- Subject is resting supine for 10 minutes.
- Data is recorded as done during baseline recording.

Trial over: -

7 Data annotation

Before annotating the data, the ECG recordings had 50Hz noises from the mains removed with MATLAB's IIR notch filter `iirnotch(w0,bw)` [45]. Additionally, the first 10 seconds of each recording were skipped during annotation, because of initial adjustment done by the ECG recording equipment. All ECG data used were recorded on Lead-II
AO amplitude data were converted from Volts to G by using the gain factor: 0.01936

To annotate the data, and insure ECG and SCG data are synchronised, a GUI was created in MATLAB, seen on figure 5. A row of buttons representing each annotation point, as well as the data point value showed underneath was used to save each annotated data point. Data were then saved to seperat ECG and SCG .txt files for later use. Each data recording had 20 full complexes annotated, or a total of 80 data points per fiducial point on trial days including alcohol, and 40 data points per fiducial point on the control day.
Given the project was done by one student, it was not possible to cross check data points for validation.

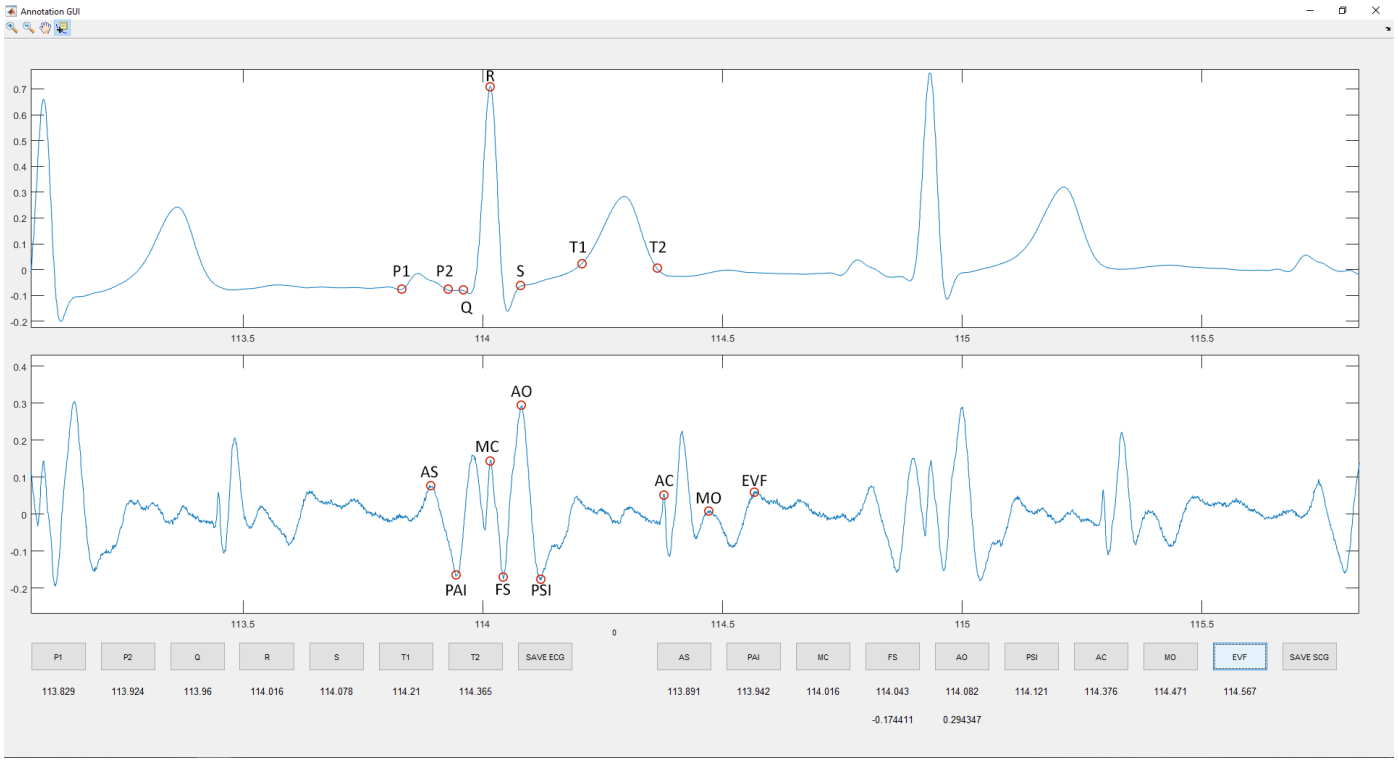

Figure 5: GUI used to annotate different fiducial points. Top graph: ECG data, annotated as P1, P2, Q, R, S, T1 and T2. Lower graph: SCG data, annotated as AS, PAI, MC, FS, AO, PSI, AC, MO and EVF

The ECG fiducial points were standardised PQRST-points seen on figure: 6, with P,Q,S and T adjusted fit the PR Interval, PR Segment, QRS Complex, ST Segment and QT Interval as seen on figure: 7. The individual fiducial points can be seen on the top graph on figure: 5

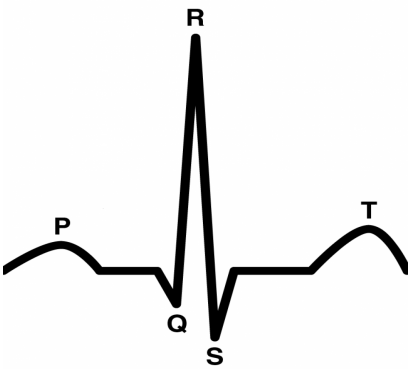

Figure 6: Representation of the P,Q,R,S,T points in a ECG. *source: https://www.researchgate.net/*

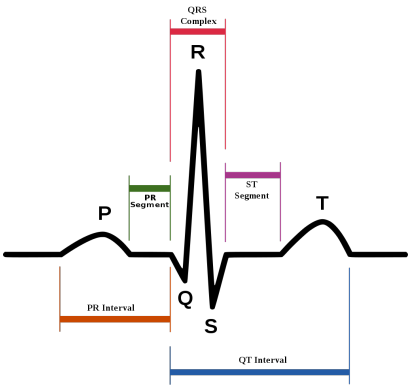

Figure 7: Representation of the PR Interval, PR Segment, QRS Complex, ST Segment and QT Interval found in a ECG. *source: https://www.researchgate.net/*

Figure 8: Caption for this figure with two images

The SCG fiducial points were chosen from a study from 2017, determining the fiducial points seen on figure 9 [11]. The vertical lines named Bs, Cs, Es, Gs, Ks, Bd, Fd and Hd were chosen to represent AS, PAI, MC, AO, PSI, AC, MO and EVF.

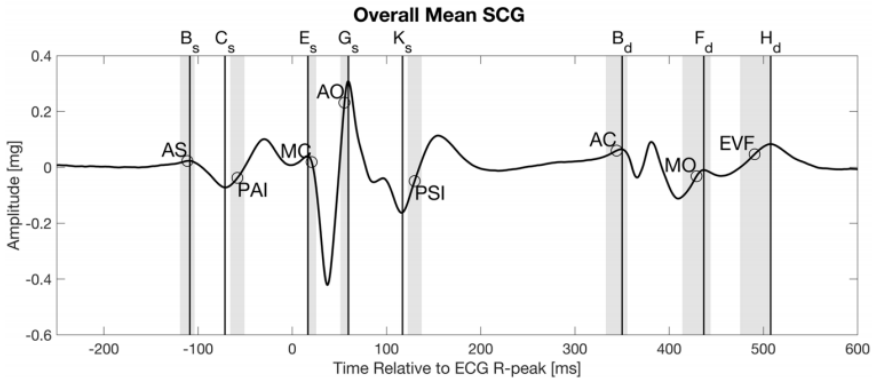

Figure 9: Representation of the SCG fiducial points. [11]

In situations where any of the above mentioned ECG- or SCG fiducial points were missing or unable to be found with certainty, the given ECG- and SCG complex were skipped. Figure: 10 shows an example of two skipped complexes because the SCG data is too noisy to use.

Figure 10: Representation of 2 skipped complexes because of noisy SCG data

7.1 Statistical method

Analysis of variance (ANOVA) is a collection of statistical models, such as the "variation" among and between groups, is used to analyse the group means differences in a sample and is based on the law of total variance, where the observed variance in a particular variable is partitioned into components attributable to different sources of variation. A simple ANOVA provides a statistical test of whether two or more population means are equal, and therefore generalises the t-test beyond two means.
For the project, repeated measures analysis of variance (repeated measures ANOVA) was chosen as stastistical model given repeated measures ANOVA is the equivalent of the one-way ANOVA, but for related, not independent groups, and is the extension of the dependent t-test. The repeated measures ANOVA is perfect test to detect overall differences between related means. [46]

8 Results

8.1 Demographics

Tabel 4 shows a list of demographic data collected from each subject.

Table 4: Table over demographic data. Data is given in percentage or as Mean (SD)

Subjects (n=2)	**Sex**	**Age**	**Weight**	**Alcohol**	**Smoking**
Subject 1	M	34	106	Moderate	Non
Subject 2	F	32	87	Moderate	Light
Mean (SD)	50%M, 50%K	23,32 (2,72)	96.5 (13,43)	100% Moderate	50% Non, 50% Light

All of the collected data is gathered in table 5 categorised after recording method. The values represent the mean value found over all subjects, with a Wilks's lambda significance in the last column. As non of the data were significant or had a Greenhouse-Geisser value of over 0.75, pairwise comparisons have been left out.

Table 5: Table of the recorded results. Mean (SD)

Segment	**Baseline**	**30 min.**	**60 min.**	**90 min.**	**P**
Blood pressure:					
Systole	130 (8.27)	135 (10.75)	137 (6.89)	139.16 (8.06)	.357
Diastole	82 (10.31)	81 (4.51)	84.5 (5.12)	85.16 (2.40)	.194
Pulse	59.66 (3.66)	65.00 (6.41)	66.33 (5.75)	62.16 (6.91)	.332
ECG:					
QRS	113.57 (11.62)	113.60 (10.15)	114.50 (13.42)	114.66 (10.71)	.188
PR interval	162.65 (7.92)	172.78 (6.14)	167.62 (7.37)	169.15 (8.7)	.788
PR segment	40.30 (5.54)	44.88 (6.78)	41.58 (7.59)	41.61 (7.01)	.225
P wave	123.01 (9.27)	124.40 (5.89)	126.03 (4.53)	125.52 (5.16)	.675
QT interval	415.12 (11.02)	408.10 (13.29)	408.06 (9.09)	412.58 (9.80)	.715
ECG and SCG:					
Q-MC	69.33 (13.70)	64.11 (8.27)	54.91 (2.33)	52.02 (3.77)	.082
PEP	136.77 (6.40)	132.43 (8.4)	123.57 (3.9)	123.19 (6.28)	.104
SCG:					
AO amplitude	8.05 (1.81)	7.59 (0.96)	7.90 (1.20)	7.45 (1.84)	.907
MC-AC	352.89 (12.45)	344.76 (16.25)	346.62 (6.79)	344.13 (7.13)	.172
MC-AO	65.28 (5.20)	65.82 (4.17)	67.00 (4.44)	66.00 (3.35)	.268
MC-PSI	106.95 (4.84)	107.20 (5.59)	109.09 (6.20)	107.53 (6.35)	.879
LVET	287.60 (12.05)	270.60 (22.31)	274.62 (17.20)	278.13 (6.33)	.223

From previous studies, we know that it is expected for the Systole, Diastole and Heart rate to rise [23]. As we see in figure 11 a rise in systolic pressure was recorded, with a steady incline from 130 (8.27) ms to 139.16 (8.06 ms) over the 90 minutes($P < 0.357$). The Diastole, seen on figure 12, also went up as expected, with a raise from 82 (10.31) ms to 85.16 (2.40) ms ($P < 0.194$)
On figure 13 The Pulse were at its peak value after 60 minutes, to then decrease again to around baseline level ($P < 0.332$). That doesn't correlate completely with what was found in previous studies, where the pulse peaked after 90 minutes.

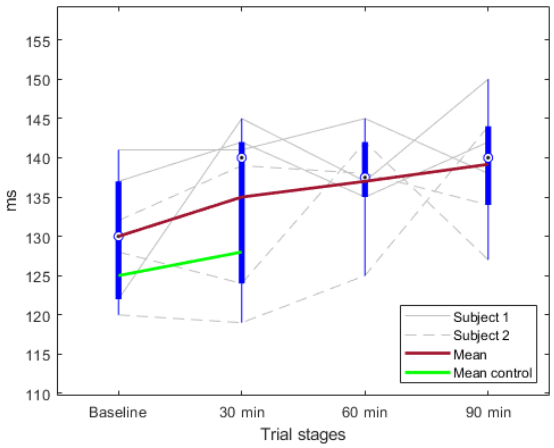

Figure 11: Systole

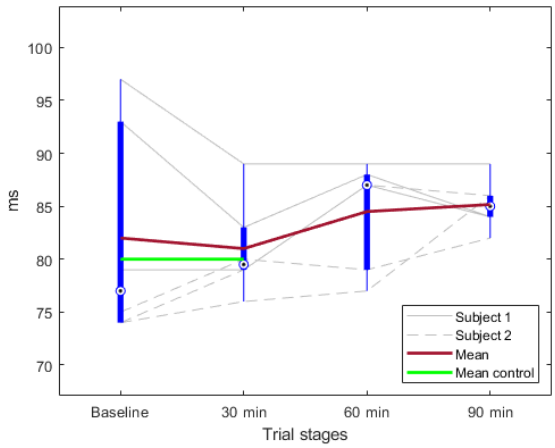

Figure 12: Diastole

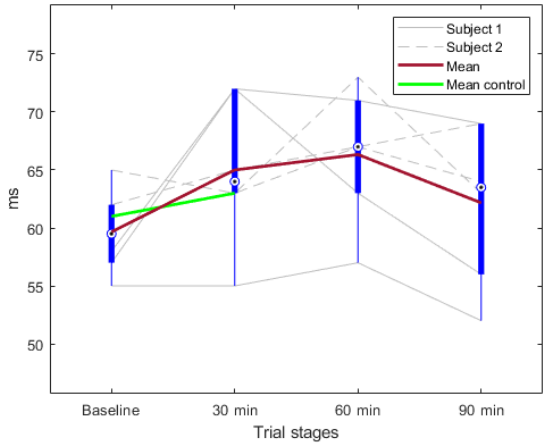

Figure 13: Pulse

On figure 14 we see the QRS timings. From literature we find that QRS timing should get longer after acute ingestion of alcohol. The QRS timing do rise, from 133.57 (11.62) ms at baseline to 114.66 (10.71) ms after 90 minutes ($P < 0.188$.)
The PR interval found of figure 15 shows a rise from baseline, just as previous studies have shown. The peak value came after 30 minutes going from 162.65 (7.92) ms to 172.78 (6.14) ms ($P < 0.788$). The PR segment seen on figure 16 showes the same tendency with a baseline of 40.30 (5.54) ms and a peak after 30 minutes of 44.88 (6.78) ms ($P < 0.225$)
On figure 17 the QT interval is shown. Previous studies found a prolonged QT interval after acute ingestion of alcohol, but this study found a decreasing QT Interval peaking at baseline 415.12 (11.02) ms falling to 408.10 (13.29) ms after 30 minutes and 408.10 (9.09) ms ($P < 0.715$)
The P wave found on figure 18 was expected to prolong and did so, with a baseline of 123.01 (9.27) ms and a peak after 60 minutes of 126.03 (4.53) ms ($P < 0.675$)

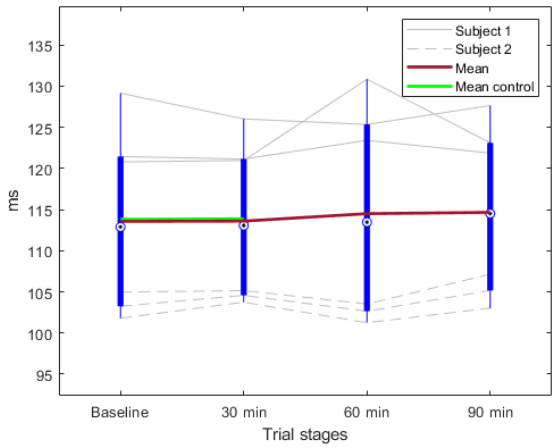

Figure 14: QRS

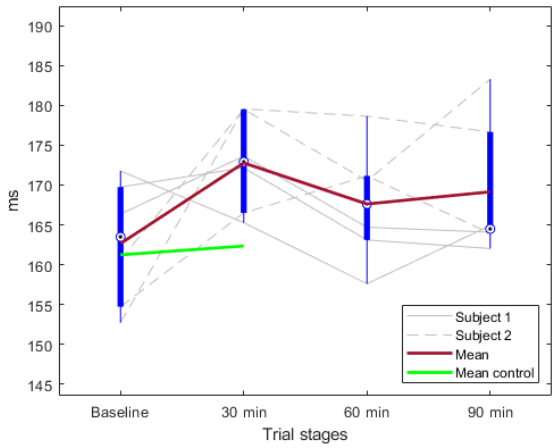

Figure 15: PR interval

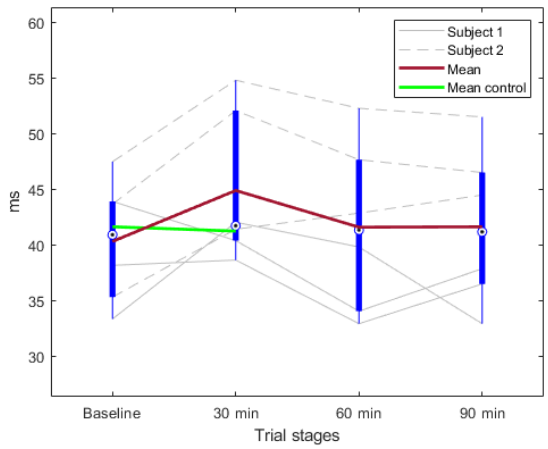

Figure 16: PR segment

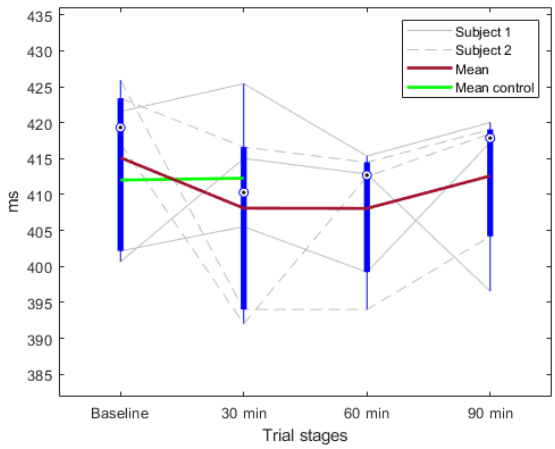

Figure 17: QT interval

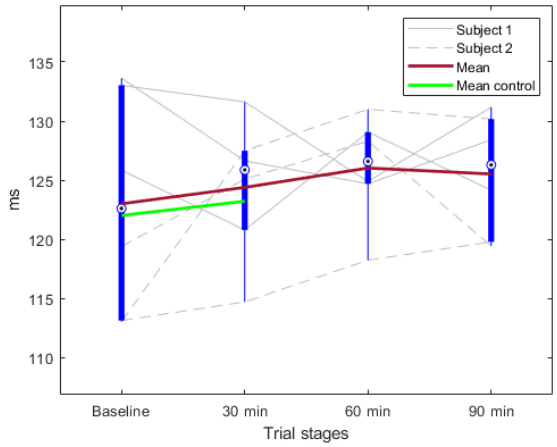

Figure 18: P wave

Studies have shown increased PEP timing after acute ingestion of alcohol, but in both cases of PEP or Q-MC which is part of PEP showed a decrease. The PEP values peaked at baseline 136.77 (6.40) ms and its lowest after 90 minutes 123.19 (6.28) ms ($P < 0.104$).

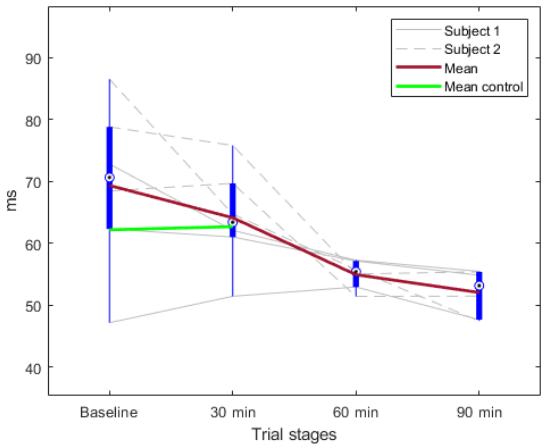

Figure 19: Q-MC

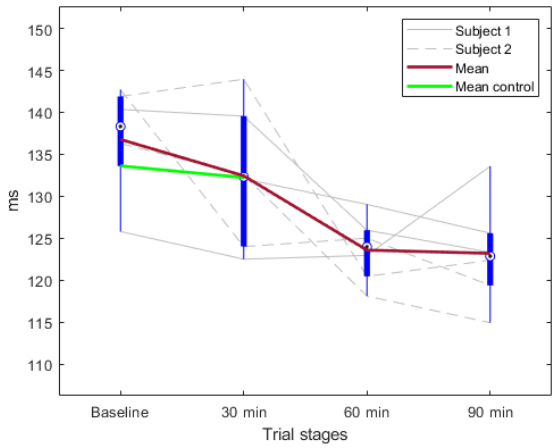

Figure 20: PEP

From previous studies it was expected for the AO amplitude to fall as the blood alcohol level was rising. Peaking at baseline 8.05 (1.81) milli-g decreasing to 7.45 (1.84) milli-g after 90 minutes ($P < 0.907$). MC-AC seen on figure 22 also declined from baseline to 90 minutes ($P < 0.172$) MC-AO seen on figure 23 and MC-PSI seen og figure 24 both rose slightly even though PEP fell. ($P < 0.268$), ($P < 0.879$) LVET fell as expected from peak at baseline 287.60 (12.05) ms to its lowest after 30 minutes 270.60 (22.31) ms ($P < 0.223$)

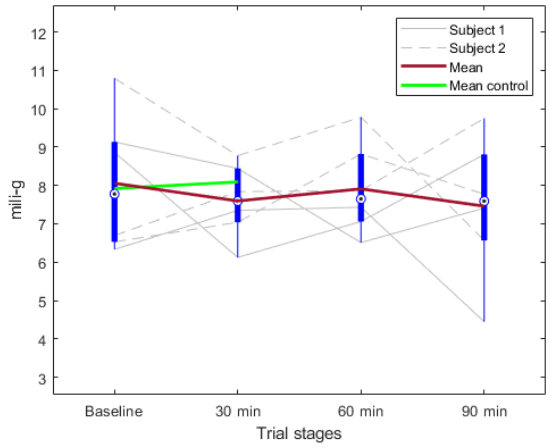

Figure 21: AO amplitude

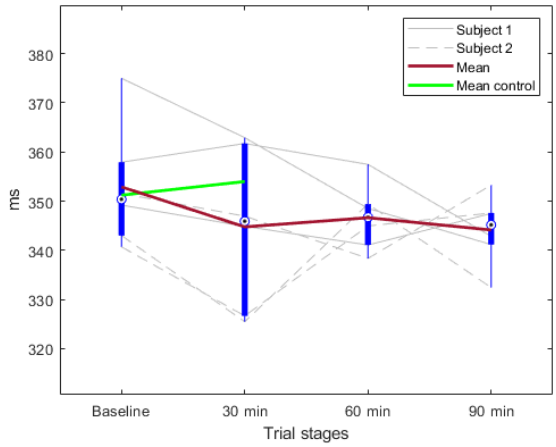

Figure 22: MC-AC

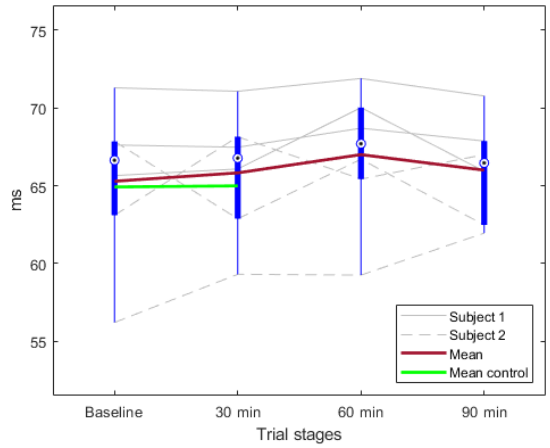

Figure 23: MC-AO

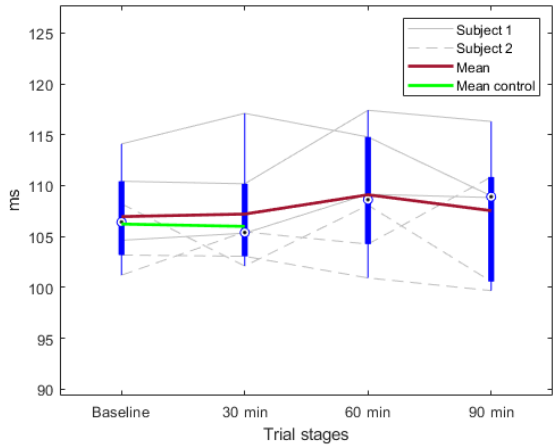

Figure 24: MC-PSI

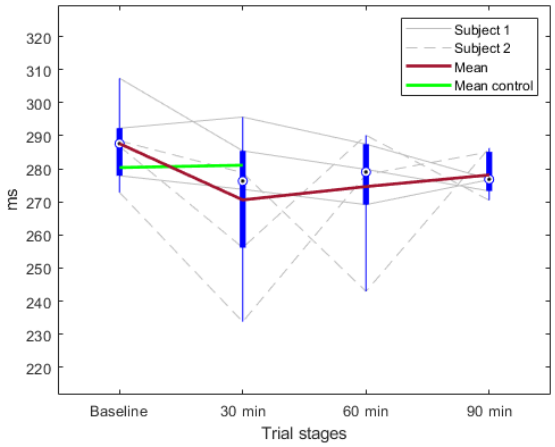

Figure 25: LVET

9 Method discussion

9.1 Sample size too small

The first issue with this experiment is the issue of sample size. This study could not utilise a sufficient sample size, due to restrictions imposed throughout the Covid19 lockdown. Therefore only two test subjects were able to participate in this study. This immediately presents concerns in terms of the reliability and indeed worth of the result. Firstly, it fails to avoid Type II errors. Due to the sample size being so small there was an increased likelihood that the results can confirm the hypothesis on which the study was based, or even show the opposite. This increases the chance of assuming as true a false premise.
In this instance the sample size is too small, thus increases the likelihood of a Type II error skewing the results. Thus these results cannot serve as a parameter on which to extrapolate reliable statistical analysis and decreases the power of the study. [47] Secondly the margin of error is highly affected by the decreased sample size. sample size and margin of error have an inverse relationship; As the sample size increases, the margin of error decreases. (the two move in opposite directions) conversely a sample size that is too large can, after a certain point, have a diminished return. Big issues in the margin of error are presented with a sample size of only two. This means observations and indeed correlations in those results are due to chance and therefore not clinically relevant. If this study were to be conducted again, there are several things that could be implemented in order to procure a far more reliable result. For example, a pilot study would be needed. This would allow statistical data to be collected on a small number of participants.

9.2 Reduced alcohol dose from 1g/kg to 0.5g/kg

Studies involving the consumption of intoxicants, drugs or other products that may have an adverse effect on the proper functioning of people or their sobriety must be considered carefully. This study invited participants to consume quite a large volume of alcohol within a short space of time and therefore consideration needed to be given to the optimal dosage. Previous studies involving the intoxication of participants have dosed 1g of alcohol for every 1kilogram they weigh. This means - based on the average weight of a Danish person – they would consume 84g over the period of an hour during this experiment. However, in this study, that amount was halved, to just 0.5g of alcohol for every 1kilogram. This would result in the averaged weighted Dane consuming just 42g over the period of an hour during this experiment. A number of factors influenced the decision to set the level of alcohol consumed at 0.5g/kg and not 1g/kg. This study was not conducted under laboratory conditions. Practically speaking this meant beds, equipment, a professional setting and even safety equipment were not available. Consuming the greater amount of alcohol would have presented higher risks to personal safety without many of the tools needed to conduct the experiment prudently. Another influential factor in reducing the amount of alcohol consumed is due to the fact there were only two participants, one of whom was the researcher and the other being the assistant to the research. Lockdown restrictions meant sourcing external participants, or even using university facilities was not an option. The levels of alcohol consumed by the two participants had to be conducive to levels of sobriety needed to conduct the experiment with as little error - due to effects of intoxication- as possible.

9.3 Errors in recording data

An addendum to this is also the concern over the reliability of the setup, results recorded and collected of the study. While it was the aim and intention to reduce errors in the set up and recording of data, this could not be assured and in some instances, owing to both test subjects also being involved in the administration of the test, it is highly likely some errors were made.
For example, at times it was necessary to remove and reapply an electrode (if the pad pulled on the skin uncomfortably after a while for instance) Due to the levels of intoxication, these could have been placed in a different position than previously, could have been placed in an incorrect place or not placed properly on the body at all. This would have a direct impact upon the measurements and results. While that impact might not produce wildly varying results, it could well produce inconsistencies that render the data more unreliable. Moreover, the timings in between each data collection point were incredibly difficult to keep. The principal was to test each subject at a thirty, sixty and ninety minute interval after the initial sixty minutes allocated for the consumption of the alcohol. This proved very difficult to adhere to, mainly owing to the fact that both participants were also required to set up and record the others results. These shifting roles resulted in delays in some instances, of up to ten minutes, which could have significant implications on the validity of the data recorded in two ways: Significant in relation to each participant, i.e. the data recorded at the thirty minute interval, may well be different, if recorded after 40 minutes, owing to a ten minute delay. Significant also to the ability to even draw minimal comparisons between participants too, if there are not recorded at the same intervals. With full access to beds, equipment and a dedicated researcher protocol would allow greater accuracy of results, owing to the fact the sober researcher can focus purely on the highest quality of administration in the tests, under the correct conditions.

9.4 Random sampling

In any experiment, the methods used to source your sample are of great importance. If the sample is to big or too small, too narrow or too wide, immediately its efficacy is under threat.
A sample size of two hits issues immediately and not just due to the very small number of the subjects as discussed under sample size. Firstly one subject was male, the other female. While both are of a similar age the fundamental principal applies where results of men cannot be extrapolated to women, or indeed vice versa. And not least with only one participant of each sex. The individualities of the participants also factors heavily on the reliability of results. The female participant identified as a smoker. While they only define themselves as a light smoker, it is well documented that smoking has effects upon factors such as heart rate, 1 cigarette per day was associated with higher resting heart rate (0.21 bpm; 95% confidence interval 0.19; 0.24) and slightly higher diastolic and systolic blood pressure (0.05 mm Hg; 95% confidence interval 0.02; 0.08) (0.08 mm Hg; 95% confidence interval 0.03; 0.13) Effect of Smoking on Blood Pressure and Resting Heart Rate A Mendelian Randomization Meta-Analysis in the CARTA Consortium - Allan Linneberg [48] With no other smokers to compare against, with no other females to compare with or indeed anyone of a similar age, diet, or weight the data collected presents a paradox. The data could indeed show the participant records results that prove to be “typical” but this cannot be extrapolated as any form of reliable conclusion, given the only comparable results were from just one other participant, who was a male non smoker. Indeed, with a sample size of just two, this is the common place problem of reliability in this study. The sample size is too small and too diverse within itself to be reliable. The demographic is simply too narrow. A larger sample of participants would

be the only sure method to reliably extrapolate results in this study
With care given to ensuring a suitable sample size of participants, such as calculating the Z-score (as previously discussed) but also ensuring participants are not overly or underrepresented in the final selection. For example, achieving a balance (as much as possible) between the number of male and female participants. A balance with regards to age, weight and other lifestyle factors, such as smoking, drug use or medical conditions. In this way, issues of narrow sampling could be overcome, creating a far more reliable basis for deducing patterns, trends and overall validity of conclusions.
Reliability and functionality of equipment. Concerns over the reliability and functionality of the equipment used in the study also posed challenges to the validity of results. Naturally, any study should incorporate strong levels of consistency. For instance, using the same electrodes, participants laying in the same position, the same software and the same machinery to record data. This all works to eliminate as many anomalous results as possible. After executing two complete sessions of data the machine used stopped working. This resulted in another machine having to be found, which unfortunately was a different model to the first, initial one. While both machines did basically the same job an important factor to note is that the age and range of functions of these machines was very different. The former being many years old, with limited function and the latter being a far more sophisticated machine, capable of much more than the first. This resulted in the first two complete data collection studies being scrapped and all subsequent data was then gathered through the new machine.
This speaks to some validity in the study at least, as using data sets from two different machines would have caused more speculation as to the validity of results. If we assume for a moment that the sample size had in fact been adequate, the issue of having to change machinery would have also had an impact. Test subjects would have been required to dedicate more of their time to the experiments, to drink more alcohol than intended and to potentially caused the researcher to expend greater finances on conducting the experiment too. Certainly the prospect of having to repeat an experiment that required a participant to again consume those levels of alcohol more times that they had initially expected could also cause some to drop out of the experiment. While this wasn't the case, as only two participants engaged in the study, it would present very real concerns for the reliability and efficacy of results, if participants dropped out, owning to a failure in technology. Failsafe's could be inserted into this part of the process however. For instance having a duplicate machine, of the same make, year and model. This would ensure that if the technology were to fail for any reason, the results collected using the second (back up) machine would be materially the same as the first, thus reliability would still follow.

10 Result discussion and conclusion

In conclusion most of the values obtained followed what had been found before and what would be expected.
The QT interval fell, but so did the PEP and LVET value. For the other mechanical SCG values they all showed noticeable changes after the ingestion of alcohol, meaning that Seismocardiography can be used to monitor changes to the hemodynamics caused by alcohol. As the study done in dogs show, the EF value can be estimated from the AO amplitude and as this study show, a changes does happen to the AO amplitude. Even though non of the results were significant, they still showed the expected changes. During settings where only ECG is available, SCG could be used not only as a stand-alone data gathering, but also as an add-on to ECG data, showing early signs of possible heart failure the ECG is not showing.

References

[1] J W Gordon. "Certain Molar Movements of the Human Body produced by the Circulation of the Blood." In: *Journal of anatomy and physiology* 11.Pt 3 (1877), pp. 533–6. URL: http://www.ncbi.nlm.nih.gov/pubmed/17231163%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC1309740.

[2] O N T H E Estimation et al. "STUDIES ON THE ESTIMATION OF CARDIAC OUPTUT IN MAN, AND OF ABNORMALITIES IN CARDIAC FUNCTION, FROM THE HEART'S RECOIL AND THE BLOOD'S IMPACTS; THE BALLISTOCARDIOGRAM". In: 127.1933 (1939), pp. 1–28.

[3] Isaac Starr and Francis Clark Wood. "on the Table, So That the Method Is Well Adapted for the Investigation of Ill Persons." In: (1942).

[4] M. MOSER et al. "The ballistocardiogram in myocardial infarction: a study of one hundred cases." In: *Circulation* 6.3 (1952), pp. 402–407.

[5] H. MANDELBAUM and R. A. MANDELBAUM. "Studies utilizing the portable electromagnetic ballistocardiograph. IV. The clinical significance of serial ballistocardiograms following acute myocardial infarction." In: *Circulation* 7.6 (1953), pp. 910–915.

[6] BS Bozhenko. "Seismocardiography–a new method in the study of functional conditions of the heart". In: *Ter Arkh* 33.Sep (1961), pp. 55–64.

[7] Laurent Giovangrandi et al. "Ballistocardiography - A method worth revisiting". In: *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS* (2011), pp. 4279–4282.

[8] David M. Salerno and John Zanetti. "Seismocardiography for Monitoring Changes in Left Ventricular Function during Ischemia". In: *Chest* 100.4 (Oct. 1991), pp. 991–993. URL: https://linkinghub.elsevier.com/retrieve/pii/S0012369216324904.

[9] Omer T. Inan et al. "Ballistocardiography and Seismocardiography: A Review of Recent Advances". In: *IEEE Journal of Biomedical and Health Informatics* 19.4 (July 2015), pp. 1414–1427. URL: http://ieeexplore.ieee.org/document/6916998/.

[10] Samuel E Schmidt et al. "Three-Dimensional Apex-Seismocardiography". In: 1221 (2014), pp. 1105–1108.

[11] Kasper Soerensen et al. "Challenges in using seismocardiography for blood pressure monitoring". In: *Computing in Cardiology* 44 (2017), pp. 1–4.

[12] Kasper Sørensen et al. "Definition of Fiducial Points in the Normal Seismocardiogram". In: *Scientific Reports* 8.1 (Dec. 2018), pp. 1–11.

[13] Kim Munck et al. "Visualization of the Multichannel Seismocardiogram Results Color plots". In: 46 (2019), pp. 1–4.

[14] Richard A. Wilson et al. "Diagnostic accuracy of seismocardiography compared with electrocardiography for the anatomic and physiologic diagnosis of coronary artery disease during exercise testing". In: *The American Journal of Cardiology* 71.7 (1993), pp. 536–545.

[15] Marco Di Rienzo et al. "A wearable system for the seismocardiogram assessment in daily life conditions". In: *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS* (2011), pp. 4263–4266.

[16] Parastoo Dehkordi et al. "Comparison of Different Methods for Estimating Cardiac Timings: A Comprehensive Multimodal Echocardiography Investigation". In: *Frontiers in Physiology* 10.August (2019).

[17] Mary A. Cardy et al. “Acute effects of ethanol ingestion on signal-averaged electrocardiograms”. In: *American Journal of Cardiology* 77.15 (1996), pp. 1356–1357.

[18] Hüseyin Uyarel et al. “Acute alcohol intake and P-wave dispersion in healthy men”. In: *Anadolu Kardiyoloji Dergisi* 5.4 (2005), pp. 289–293.

[19] Willy Aasebø et al. “EGG changes in patients with acute ethanol intoxication”. In: *Scandinavian Cardiovascular Journal* 41.2 (2007), pp. 79–84.

[20] Hitesh Raheja et al. “Electrocardiogram Changes with Acute Alcohol Intoxication: A Systematic Review”. In: *The Open Cardiovascular Medicine Journal* 12.1 (2018), pp. 1–6.

[21] Howard S. Friedman. “Cardiovascular effects of alcohol with particular reference to the heart”. In: *Alcohol* 1.4 (1984), pp. 333–339.

[22] Philip O. Ettinger et al. “Arrhythmias and the ”Holiday Heart”: Alcoholassociated cardiac rhythm disorders”. In: *American Heart Journal* 95.5 (1978), pp. 555–562.

[23] Jonas Spaak et al. “Dose-related effects of red wine and alcohol on hemodynamics, sympathetic nerve activity, and arterial diameter”. In: *American Journal of Physiology - Heart and Circulatory Physiology* 294.2 (2008), pp. 605–612.

[24] Zhibin Cong et al. “A potentially new phase of the cardiac cycle: Pre-isovolumic contraction recognized by echocardiography”. In: *Medicine (United States)* 97.21 (2018), pp. 1–6.

[25] Erika Ecker and Andrea Skelly. “Conducting a winning literature search”. In: *Evidence-Based Spine-Care Journal* 1.01 (May 2010), pp. 9–14. URL: http://www.thieme-connect.de/DOI/DOI?10.1055/s-0028-1100887.

[26] NCBI. *MeSH*. 2019. URL: https://www.ncbi.nlm.nih.gov/mesh.

[27] National Videnskabsetisk Komité. *Forskertjeklister — National Videnskabsetisk Komité*. URL: http://www.nvk.dk/forsker/forskertjeklister.

[28] Rima Abu-Amsha Caccetta et al. “Red wine polyphenols, in the absence of alcohol, reduce lipid peroxidative stress in smoking subjects”. In: *Free Radical Biology and Medicine* 30.6 (Mar. 2001), pp. 636–642.

[29] John G. Webster. *Medical Instrumentation Application and Design*. 4th ed. John Wiley & Sons, Ltd (10.1111), 2010, p. 713.

[30] Amirtahà Taebi et al. “Recent Advances in Seismocardiography”. In: *Vibration* 2.1 (2019), pp. 64–86.

[31] Mark W. Maciejewski et al. “Nonuniform sampling and spectral aliasing”. In: *Journal of Magnetic Resonance* 199.1 (July 2009), pp. 88–93. URL: https://linkinghub.elsevier.com/retrieve/pii/S1090780709001037.

[32] IWorx. *iWorx — IX-ECG12 12-Lead ECG Recorder with LabScribe Software*. 2020. URL: https://www.iworx.com/products/data-recorders/12-lead-ecg-recorder-labscribe2-software/.

[33] IWorx. *iWorx — IX-RA-834 10+ Channel Recorder and Stimulator*. 2020. URL: https://www.iworx.com/products/data-recorders/ix-ra-834-8-channel-recorder/.

[34] F. Landreani et al. “Beat-to-beat heart rate detection by smartphone’s accelerometers: Validation with ECG”. In: *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*. IEEE, Aug. 2016, pp. 525–528. URL: http://ieeexplore.ieee.org/document/7590755/.

[35] High-quality Electrodes. “From the neonatal ward to emergency defibrillation , Covidien will help”. In: (2020).

[36] Sundhedsogaeldreministeret. *Komitéloven - Bekendtgørelse af lov om videnskabsetisk behandling af sundhedsvidenskabelige forskningsprojekter - retsinformation.dk*. 2017. URL: https://www.retsinformation.dk/Forms/r0710.aspx?id=192671.

[37] Nationalvidenskabetiskkomitedinerettighedersomforsoegsperson. *Dine rettigheder som forsøgsperson — National Videnskabsetisk Komité*. URL: http://www.nvk.dk/forsoegsperson/dine-rettigheder-som-forsoegsperson.

[38] World Medical Association. *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects – WMA – The World Medical Association*. URL: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.

[39] Datatilsynet. *Datatilsynet*. 2019. URL: https://www.datatilsynet.dk/.

[40] Europa Parlamentets og Rådets Forordning. *EUROPA-PARLAMENTETS OG RÅDETS FORORDNING (EU) Nr. 536/2014 af 16. april 2014 om kliniske forsøg med humanmedicinske lægemidler og om ophævelse af direktiv 2001/20/EF (EØS-relevant tekst)*. (EU) Nr. 536/2014, 2014. URL: https://eur-lex.europa.eu/legal-content/DA/TXT/PDF/?uri=OJ:JOL_2014_158_R_0001&from=DA.

[41] Sundhedsstyrelsen. *Sundhedsstyrelsens anbefalinger om alkohol — Alkohol & Samfund*. 2020. URL: https://alkohologsamfund.dk/alkopedia/sundhedsstyrelsens-anbefalinger-om-alkohol.

[42] IWorx. *iWorx C-ISO-SL5*. 2020. URL: https://iworx.com/zencart/index.php?main_page=product_info&products_model=C-ISO-SL5.

[43] iWorx. *iWorx — LabScribe v4*. 2019. URL: https://www.iworx.com/research/software/labscribe/.

[44] van de Borne Philippe et al. "Effects of Alcohol on Sympathetic Activity, Hemodynamics, and Chemoreflex Sensitivity". In: *Hypertension* ().

[45] MathWorks. *Second-order IIR notch filter - MATLAB iirnotch - MathWorks Nordic*. 2019. URL: https://se.mathworks.com/help/dsp/ref/iirnotch.html.

[46] Laerd Statistics. *Repeated Measures ANOVA - Understanding a Repeated Measures ANOVA — Laerd Statistics*. 2020. URL: https://statistics.laerd.com/statistical-guides/repeated-measures-anova-statistical-guide.php.

[47] PennState. *2.3 - Relationship between Sample Size and Margin of Error — STAT 100*. 2020. URL: https://online.stat.psu.edu/stat100/lesson/2/2.3.

[48] Allan Linneberg et al. "Effect of Smoking on Blood Pressure and Resting Heart Rate: A Mendelian Randomization Meta-Analysis in the CARTA Consortium". In: *Circulation: Cardiovascular Genetics* 8.6 (Dec. 2015), pp. 832–841. URL: https://www.ahajournals.org/doi/10.1161/CIRCGENETICS.115.001225.