NHS Foundation Trust

CENTRE FOR HEALTH RESEARCH AND INNOVATION

Protocol

Title:
MyPad – Intelligent Bladder Pre-void Alerting System

Study Team & Collaborations:

Chief investigator: Dr Christian De Goede, Consultant Paediatric Neurologist, Lancashire Teaching Hospitals NHS Trust. Christian is a consultant paediatric neurologist with a keen interest in research, working closely with local universities. He has an interest in the use of technology in clinical practice, and for example is involved in a project developing a wearable EEG device. Christian will lead the clinical side of the project with his team as a principal investigator.

Dr Darren Ansell, research lead, University of Central Lancashire. Darren is the engineering lead in the School of Engineering. He specialises in applied autonomous and intelligent systems research. Darren completed his PhD at Cranfield University in 2005 in electronics. He has several patents. He has contributed significantly to the preparation of My-PAD published patent. Darren will manage the technical side of the project and is involved in all work packages

Dr Kaya Kuru, research associate, University of Central Lancashire. Kaya is a research associate at the School of Engineering. He completed his Ph.D in computer science/medical informatics at Middle East Technical University. He developed several novel techniques in My- PAD project and My-PAD smartphone SW application based on these techniques. He has contributed significantly to the preparation of My-PAD published patent.

Martin Jones, Researcher, University of Central Lancashire. Martin is an Innovation and R&D manager within the School of Engineering, specialising in Industrial Design and Human Factors research methods. He has an MA in Industrial Design. He has directed several wearable support garment designs to keep the US device in firm contact with the body, and in an optimum position for obtaining bladder measurements for both sexes and population morphology types. He will support the device usability and product design development aspects.

Mairi Oliver, Researcher, University of Central Lancashire. Mairi is a Research Assistant in the School of Engineering, with a BSc in Industrial Design. She is working on a portfolio of patent applied for medical technologies and devices. She has worked on designing several wearable support garments to keep the US device in firm contact with the body, and in an optimum position for obtaining bladder measurements for both sexes and population morphology types. She will support the development of the physical product aspects and implement findings across the work packages.

Benjamin Jon Watkinson, Research Associate, University of Central Lancashire. Ben is a research associate in the school of engineering with an MEng in Robotics Engineering. He is currently working on a range of projects, including development of medical devices. He will be supporting the electronic design aspects of the project.

Peter Leather, Commercialisation Manager, University of Central Lancashire. Peter is Head of Intellectual Property & Commercialisation. He is skilled in connecting people, ideas and resources at different parts of the innovation process. He is also skilled at

applying technology and technical insight that help turn ideas into successful products and services. He has contributed significantly to the preparation of My-PAD published patent. He will be assisting the project through IP and commercialisation aspects.

Dr Chooi Oh, Consultant Radiologist, Lancashire Teaching Hospitals NHS Trust. He is a consultant radiologist with a large research interest. He will provide advice and support around clinical use of ultrasound in particular in measuring bladder volume.

Dr Pijush Das, Consultant Community Paediatrician, Lancashire Teaching Hospitals NHS Trust. He is a child health consultant at Royal Preston Hospital. He will provide clinical expertise to the project.

Tracy Ann Lofthouse, paediatric outreach sister, enuresis, Lancashire Teaching Hospitals NHS Trust. She is a nurse in Child Health Department at Royal Preston Hospital. She is primary specialised in the treatment of children with NE. She will help establish new PPI groups to carry out the EBCD approach throughout the project, in particular in supporting the testing phases.

Paula Sugden, paediatric outreach sister, enuresis, Lancashire Teaching Hospitals NHS Trust. She is a nurse in Child Health Department at Royal Preston Hospital. She is primary specialised in the treatment of children with NE. She will help establish new PPI groups to carry out the EBCD approach throughout the project, in particular in supporting the testing phases.

Kina Bennett, research operations manager, Lancashire Teaching Hospitals NHS Trust

Background *(Literature review):*

Nocturnal enuresis (NE) is the involuntary discharge of urine at night in the absence of congenital or acquired defects of the central nervous system or urinary tract. NE is a widespread and distressing condition that can have a deep impact on a child or young person's behaviour, emotional wellbeing and social life along with parental intolerance; it is also very stressful for the parents or carers [1,2]. Many people never seek help because they are too embarrassed, and some people wet the bed regularly all their lives. Bed wetting causes many practical problems, such as constantly having to change wet sheets and bedding with associated laundry costs. Bed wetting can affect sleep patterns and often causes frustration and exhaustion for the family. NE can affect normal daily routines and social activities such as sleep-overs or school trips. It can also affect self-esteem and generate much more serious feelings and behaviours, such as a sense of helplessness and a lack of hope and optimism[3], feelings of being different from others, feelings of guilt and shame, humiliation, victimisation and loss of self-esteem[4,5,6].

Most children will become dry eventually, but in some children this development is delayed, and by the age of 5 approximately 10% of children still wet the bed, and by age 10 the figure is around 5%. The reason for this delay is uncertain, but there are ways to help children and families. Persistence of bed wetting into adolescence is likely to be accompanied by ridicule and bullying by peers and increased intolerance from parents, especially if they believe that their child is to blame for the problem. Such reactions can only serve to exacerbate the young person's distress and may lead to

delays in seeking help. In particular, teenagers who are unsuccessfully treated in childhood are often reluctant to seek help due to the severe embarrassment associated with the problem, and others may simply believe that no help is available [2]. The treatment of bedwetting has a positive effect on the self-esteem of children and young people [2,6,7] .

As evidenced by the PCF (The British Association of Social Workers (BASW) Professional Capabilities Framework) access to professionals with a specialist interest in this field is declining as a result of commissioning priorities. Many areas across the UK are also losing paediatric continence teams, continence nurses or specialist physiotherapists. The erosion of the school nursing role has impacted on this area significantly with many families unable to access appropriate support, advice and management according to PCF.

NICE has recommended use of a bed alarm as first line management, with medication as an alternative [8]. Moisture detection alarm is offered by NICE as a first-line treatment for a period ranging from 4 weeks to 3 months depending on the dry nights; desmopressin is less preferred but may be considered if the child, parents, or carers do not want to use an alarm or are unable to use an alarm for a period ranging from 3 to 6 months; sometimes, combination treatment with desmopressin and an enuresis alarm is offered; tricyclic antidepressants may be offered by an expert if all approaches above are not successful; bedwetting may recur after being treated successfully (14 consecutive dry nights) by either moisture detection alarm or medicine [8]. Dry bed training is not recommended because there is very-poor-quality evidence to support its use and because, as part of dry bed training, the child may be punished [8]. Furthermore, many families consider the use of complementary and/or alternative medicine (CAM) such as acupuncture and hypnotherapy as a treatment option when conventional treatment fails or in order to avoid drug or other treatments [2]. There is very little evidence about the efficacy of many complementary and/or alternative medicine (CAM) treatments, but the use of CAM is widespread and increasing across the developed world [2] based on unsuccessful treatment results of the current methods.

This is a pre-clinical study. We aim to develop an effective pre-void alarm to manage the NE, which would be more acceptable than currently available alarms. The use of alarms for management of NE has been in practice for just over a century [9,10]. While technology has advanced, the basic principle of the approach has remained more or less unchanged, alerting the child at the point of voiding, when the wetting is happening or has happened. This still results in extra laundry and interrupted family sleep patterns until the child has learned to control the bladder. If children and families are to be motivated to use an alarm system to improve NE the system needs to be accessible, affordable and effective at minimising wetting by inhibiting the event of a wet bed, by early alerting. The system needs to be easy to use with data intuitively informing individual management approach and alerting when to seek further advice from health professionals. My-PAD project was developed to explore whether existing technologies could be synchronised, enhanced and modulated to form an intelligent alarm system that could provide a pre-void warning, minimising bedwetting, reaching stable dryness through learning bladder control and enhancing quality of life for sufferers.

Research Objective:

1. Produce an effective pre-void alarm system that wakes the child before voiding

2. Develop an enuresis alarm that is comfortable to wear – design of alarm and garment acceptable to children and young people to wear at night.

Objectives and Specific Aims:

The aim of this project is to build, refine and evaluate a new safe, comfortable and non-invasive wearable intelligent electronic device to monitor the bladder and to treat NE by warning the patient at the pre- void stage, enhancing quality of life for these sufferers starting from the first use. No such technology exists currently to monitor bladder to alarm before bedwetting.

The device will measure several parameters of the human urinary bladder using a frequency modulated ultrasonic signal. An US (ultrasound) sensor adheres to abdominal skin area over the bladder, transmitting pulses through the anterior bladder wall to detect the necessary immediate features of the bladder using the echoed attenuation signals from a bladder. It will also log and use movement, temperature and moisture measurements to enhance the warning performance. The device can set a customised warning trigger based on the bladder expansion cycle with respect to the likelihood of an imminent voiding of the bladder by learning the bladder characteristics specific to users automatically.

The project builds upon earlier work which has developed software that understands US scan data and can issue warnings at several particular bladder urine volume levels. The project will produce the device's electronic circuitry (by modification to existing small form factor US devices) - a low power portable US sensor, movement sensors, moisture detectors and event logging buttons so that voiding and drinking events can be recorded by the user. The device will have a Bluetooth® connection to establish a wireless functionality between the device and smartphone application. The device can also record a voiding event through the device's moisture sensor detecting wetness in the case of an involuntary voiding event to customise itself for the current user in terms of the triggering threshold using self-tuning features. The device casing and a garment for holding the device in the correct place on the body will also be manufactured and evaluated for comfort, usability and practicality. The garment can be separated from the device to be washed.

The key aims for the project are:
i) Optimise the device ultrasound performance (technical)
ii) Produce a practical wearable device acceptable to children,
iii) Conduct user trials to evaluate reliability, gather data to support the operating concept, and gain early indications of efficacy,
iv) Reach a pre-production prototype stage

Rationale and Significance of Study:

Unsatisfactory cure rates with currently available treatments of NE have led to the need to explore alternative modalities. New treatment methods that focus on preventing enuretic episodes by means of a pre-void alerting system could improve outcomes for children with NE in many aspects such as voiding in a dignified manner, reducing cost, reducing time to tackle the problem, improving the psychology of the sufferers [1, 9-13]. The aim of this project is to build, refine and evaluate a new safe, comfortable and non-invasive wearable intelligent electronic device to monitor the bladder and to treat NE by warning the patient at the pre- void stage, enhancing quality of life for these sufferers starting from the first use. No such technology exists currently to monitor bladder to alarm before bedwetting.

Beyond this study, there are numerous other areas of application i.e. elder care (geriatric) settings, stroke patients [13] and veterinary science in which My-PAD can be of potential benefit.

Research Design

Technical development.

Iterative development of a comfortable, miniaturised, highly customisable, US-based device which is mounted ergonomically on a child's abdomen wall, to measure the distension of urinary bladder and consequently decides '*smartly*' whether to issue an alert to wake the patient (pre-void) during the night. Several non-invasive low powered sensors detect changes in the pattern of ultrasound pulses reflected from multiple points of the bladder and related tissue around the bladder in intermittent manner using a skin-interfacing pad, and the acquired information in a data storage unit is transmitted into a processing/computing unit *using wireless Bluetooth technology*. The discriminant features (detailed in our patent [8]) extracted from this information based on the specific characteristics of urine in the bladder and the bladder itself are then processed by the smartphone computer-implemented Machine Learning (ML) techniques in a parallel software processing to determine the relative fluid level (to at least 50ml) in the bladder. Other sensors such as movement, temperature and moisture measurements are employed to enhance warning performance and self-customising features.

For the prototype, software has been designed to decrease the intensity and ultrasound signal exposure time to the minimum. The sonar energy penetrated through the body in intermittent manner will cause no heating risk for the body in line with international guidelines and regulations of related international organisations [11]. This device will be used in a trial of wearability and usability in a group of children.

Patient involvement in design.
Throughout the project there will be focused engagement with the trial participants in group sessions and through individual interviews to gain qualitative and quantitative data and iterate the device design and functionality. The PPI groups will be established at both Royal Preston Hospital and at ERIC's location in Bristol. This will involve gathering experiences and ideas from children, their parents and staff through in-depth interviewing, observations and group discussions, identifying key 'touch points' (emotionally significant points) and assigning positive or negative feelings. The findings will inform the design and functional requirements for My-PAD device iterations. This approach will continue throughout the project at key stages and during trial and evaluation periods.

Recruitment of Participants:
Children attending the enuresis clinic at Lancashire Teaching Hospitals will be approached and invited to take part in the different phases of this project. This comprises 4 parts as further detailed below. For the first 3 parts healthy volunteers can be included.

Inclusion criteria:
-Age 7 years to 12 years
-Bedwetting twice a week or more (For the initial comfort trials and the calibration trial healthy volunteers may be invited to take part)
-Good understanding of English language

Exclusion criteria:
-there is a medical cause for bedwetting
-the child has significant learning difficulties
-the child is obese (above 98th centile for Body Mass Index)
-the child has severe hearing impairment

Methodology:

The testing of the device will be organised in 4 stages:

I. Comfort trial. 5 children attending clinic or healthy volunteers will be asked to wear a 'dummy' device (that is a box in the shape of the device, but without the technology inside) and garment. They will be asked to wear this on 7 consecutive nights. They will be asked about comfort, in particular the comfort at night and tolerance during sleep. Through interviews and questionnaires, we will ask for patient feedback on device comfort and sleep quality, and feedback on undergarment and skin attachment experience. This will further shape the device and underwear.

II. Initial testing: 5 children from clinic or healthy volunteers will be asked to wear a functional device to test if it can accurately measure the volume of the bladder, and can alarm at the appropriate time. They will be invited to spend a morning or afternoon in our Clinical Research Facility. The readings from the device will be compared with measurements obtained by a normal ultrasound machine, to calibrate the equipment. Children will be asked to drink, to ensure their bladder fills up, and at the end they will be asked to empty their bladder. This way different bladder sizes can be compared using the alarm system and a normal ultrasound machine.

III. Initial testing at night: 5 children from clinic or healthy volunteers will be asked to wear a functional device for 7 consecutive nights. This will test if the device can measure the volume of the bladder, and can alarm at the appropriate time. This will also test the best way to alert the children to wake up when the bladder is full. Volunteers for the trial will be trained on using the device and on how to wear the device properly. They will then evaluate the device over a period of a week, wearing the device at night and using an associated smart phone application to store data from the device. This part of the study will also test durability of the device and battery usage. Interviews will be held to fully capture feedback and experience of using the device. Different alarm methods will also be evaluated (randomly) to determine effective methods of awaking and alerting children at night.

IV. Efficacy Trial - longer term testing at night: After obtaining successful results from previous phases, the device will be tested on 10 children with bedwetting. In this part of the trial we aim to determine the initial efficacy of the device. We aim to find if it alarms at the right time, and in particular if we can reduce the number of wet nights. Children will be asked to wear the device at night for an extended period of 10 weeks. During this the device 'self learns' the volume of the bladder in this particular child, and learns when to alarm. There will be regular reviews to determine how the device performs at night, with an evaluation of its altering performance compared with historical patterns of bedwetting events for each individual child. Data collection will include the performance of the device, it's sensor, success rate in waking the child, reduction in wet nights. At the end of the trial, children and families will be invited to discuss the experience. Further feedback will be obtained through interview and questionnaires. A final follow up in clinic or by phone will be included to enquire about longer term success in becoming dry at night. If at the end of 10 weeks the child is not dry, the family have a choice to continue using this device for up to another 10 weeks, or to change to the available 'wet alarm' that is used in the clinic.

Data Analysis:
There will be analysis of all the measurements and technical data, to check the device and calibrate. Throughout the study, data will be stored and compared to improve the algorithms used to measure the bladder size and estimate the threshold for alarming in a specific child.

There will a qualitative approach to answers gained through interview and questionnaires around the design, use and comfort of the device. These will be used to adapt the design of the device and the garment, the best alarm to help wake the child and the usability of alarm and connected handheld device.

Dissemination:

A steering group will be formed comprising of key stakeholders from the project partners, ERIC, external clinicians and PPI representatives. The steering group will meet at least four times during the project to review progress, discuss project outcomes and success and set direction and priorities for the iterative development process. A project management team will be established for day-to-day management of the project to ensure progress, manage project risks and budget. An independent health economics study will be produced to support commercialisation efforts. Team members will conduct dissemination work at appropriate venues, events and locations to ensure study findings are shared and raise awareness of the new device.

Our dissemination strategy will begin from the start of the study through our engagement with ERIC (The Children's Bowel & Bladder Charity) who will be regularly briefed throughout the work programme. ERIC will support dissemination via their Professional Advisory Committee work, through dedicated focus groups and via training and conference attendances.
Probable further patents and high impact factor journal/conference publications will be prepared based on the performance of the device and test results acquired throughout the project.

The device and the techniques employed will be presented in a technical report on the University of Central Lancashire's public access 'Clok' system and on other related university web pages as well as via the media. The University of Central Lancashire will lead on the dissemination and exploitation activities, in particular patent preparation and publications.
In addition, an international patent has recently been published on our novel techniques, innovative US processing software and the design of the device [12].

Ethical issues:

Device
For the prototype, software has been designed to decrease the intensity and ultrasound signal exposure time to the minimum. The sonar energy penetrated through the body in intermittent manner will cause no heating risk for the body in line with international guidelines and regulations of related international organisations [11]. This device will be used in a trial of wearability and usability in a group of children. The ultrasound element used in the device has been EC marked for use.

Children
Enuresis is a sensitive topic, and children and families will be supported by our highly skilled specialist nurses throughout the research process. In the initial part of the study we aim to gather the thoughts and ideas of children and their family on the device. Children may be conscious about bedwetting, in particular in teenage years. We will offer the opportunity to either meet in a group, or as individuals with the research team, to explore their ideas on the bedwetting device and the design of the device and the garment. As the study progresses, we will ask the children to wear the device and feedback on comfort and user-friendliness. This will be organised within a clinic setting, similar to the enuresis clinic, and as such is not different from the normal clinical encounter, just that this is to try a new device, rather than the established enuresis alarm currently in use. Any distress in the children is likely related to the bedwetting, rather than the use of a different device, but the enuresis nurses, and the principal investigator, will be available to meet with the children and families to support them. If at any stage children are unhappy with the trial or the device, they/ their family can stop their involvement in the trial, and they will continue to be seen in the regular enuresis clinic for further management.

Ethical review and approval will be sought through an application through IRAS.

References:

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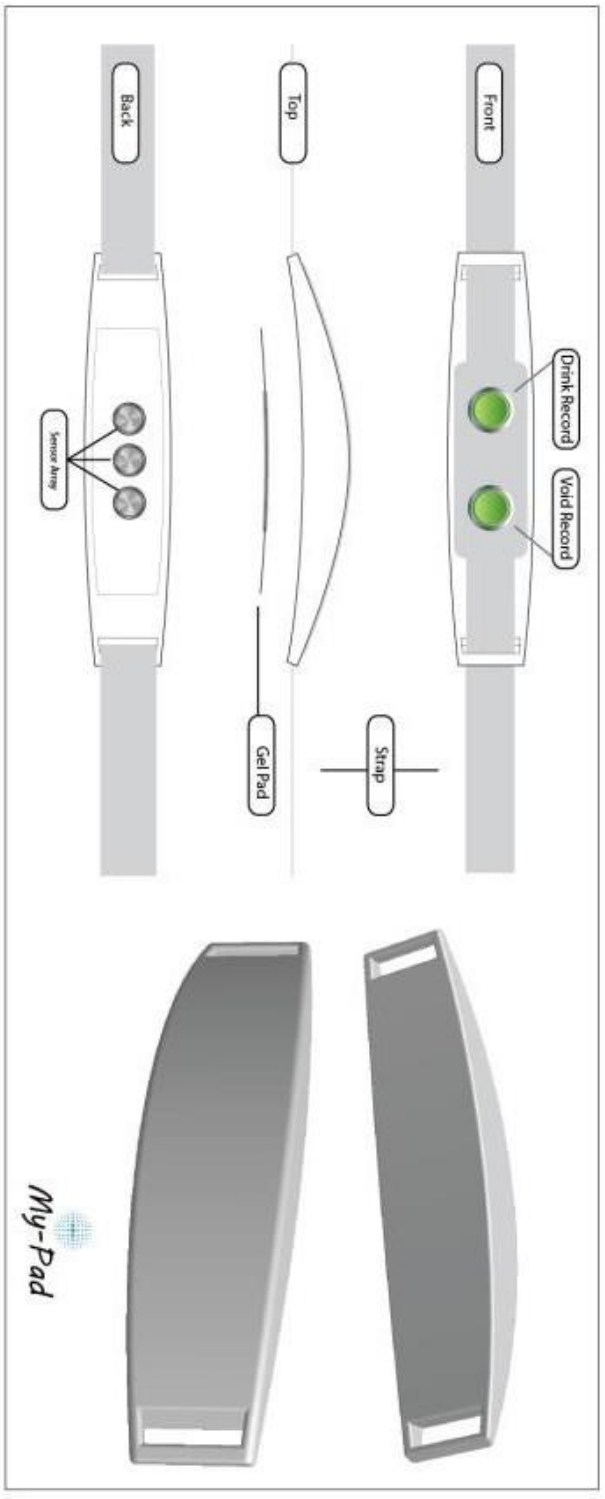
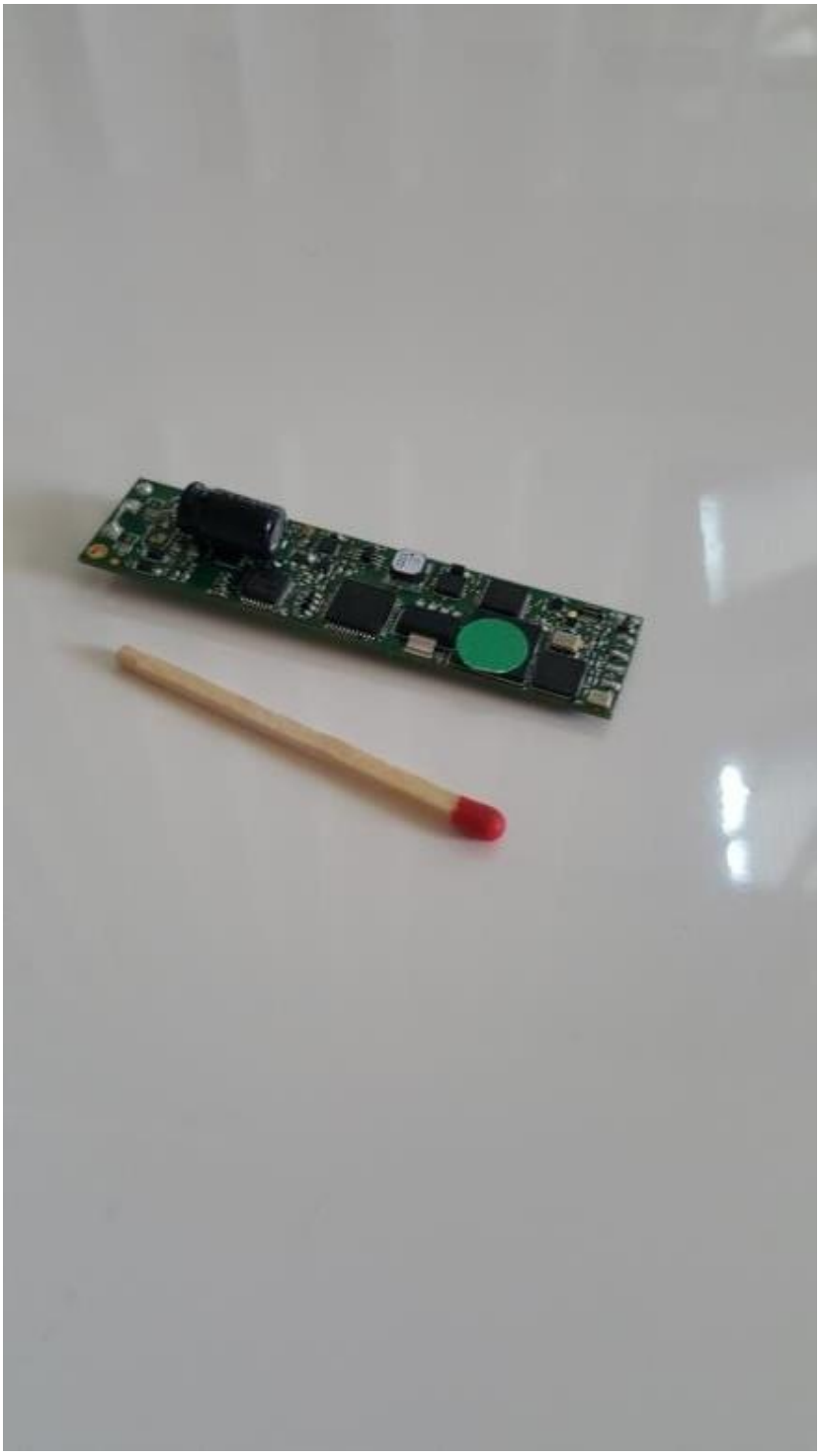


Product casing sketches.



Early version of ultrasound electronics board to give indication of scale.