Validation of a Non-Invasive Ultrasonic Patch For Continuous Blood Pressure Monitoring in Orthostatic Hypotension

Who is conducting the study, why you have been asked to participate, how you were selected, and what is the approximate number of participants in the study?

Dr. Litvan and her team are conducting a research study to validate the use of a non-invasive continuous blood pressure monitor ultrasonic patch and find out more about monitoring orthostatic hypotension (defined as a drop in systolic blood pressure (the top number) of ≥ 20 points or in diastolic blood pressure (the bottom number) of ≥ 10 points when standing upright). You have been asked to participate in this study because you are aged 18-90 years without active medical problems. There will be approximately 70 participants enrolled in this study.

Why is this study being done?

The purpose of this study is to validate the clinical application of a non-invasive, wearable continuous blood pressure monitor. The device is worn as a small patch placed on top of the skin on the front of the neck, the arm, or the wrist. The patch uses ultrasound to measure blood pressure from the arteries underneath the skin. This device is investigational, and has not been FDA-approved for marketing. We will first collect pilot data, also known as preliminary or exploratory data, to calibrate the device and optimize its wearability and accuracy. We will collect pilot data from about 10-15 people. After optimizing the device, we will recruit participants to compare the blood pressure measurements collected from the ultrasonic patch to measurements collected using a standard inflatable manual blood pressure cuff in order to validate our device.

Eventually, we plan to integrate this device with sensors that measure other physiologic information (including heart rate, temperature, position, movement, and brain and muscle activity). The long-term goal is to apply this system in clinical practice for ambulatory blood pressure monitoring, which will allow clinicians to properly assess and manage response to treatment in people with blood pressure fluctuations.

Who is eligible to participate in this study?

You ARE eligible to participate in the study if you meet the following *inclusion criteria*:

- Ages 18-90 years old
- Are able to provide informed consent
- Have at least one arm

You are NOT eligible to participate if you have any of the following *exclusion criteria*:

- Active cardiac arrhythmias
- Any other unstable, active medical condition (i.e., cardiac arrythmia, uncontrolled diabetes, active heart failure, active liver failure)
- Currently pregnant (this will be confirmed with a urine pregnancy test in women of childbearing potential)

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- Any large movements of the arms (e.g., chorea, dyskinesias, ballism), that in the investigators' opinion, would make it difficult to measure blood pressure using a standard blood pressure cuff
- Diagnosis of dementia
- Any active skin infection or wound on the arm or neck that would interfere with the devices used to measure blood pressure

Additionally, in accordance with The Institute of Electrical and Electronics Engineers (IEEE) Standard for Wearable, Cuffless Blood Pressure Measuring Devices, we will include 11 people in each of the following categories of blood pressure, based on the screening blood pressure measurements. **You may be ineligible if the investigators have already recruited a sufficient number of participants within a given blood pressure category.**

Blood Pressure Classification	Systolic Blood Pressure (mmHg)		Diastolic Blood Pressure (mmHg)
1. Hypotensive	<100	and	<70
2. Normotensive	100-119	and	70-79
3. Pre-hypertensive	120-139	or	80-89
4. Stage 1 Hypertensive	140-159	or	90-99
5. Stage 2 Hypertensive	≥160	or	≥ 100

What will happen to you in this study and which procedures are standard of care and which are experimental?

If you agree to be in this study, the following will happen to you:
During the screening visit, you will go over the informed consent forms, including review of inclusion and exclusion criteria. Before any study procedure will be performed, including screening procedures aimed to determine your eligibility, your informed consent will be obtained.

Screening visit (approximately 1 hour):
After informed consent, you will undergo the following procedures to confirm your eligibility, including:
1) Medical history collection (20 minutes)
2) Montreal Cognitive Assessment (10 minutes)
3) Clinical assessment to determine decisional capacity, evaluate any symptoms and motor function using clinical rating scales (20 minutes)
4) Blood pressure measurement (5 minutes)

Study visit (approximately 1 hour):
Once your eligibility is confirmed, you will proceed to the study procedures immediately following the screening visit on the same day.
Pilot Data Collection: We may collect pilot data, which is preliminary information. This will be used to calibrate and optimize the design of the ultrasonic blood pressure device. This would

involve quietly sitting in a chair or lying on a bed for up to an hour while your blood pressure is monitored with the test device placed on your neck, arm, or wrist. We will remove the device at the end of the visit. We may also use a non-invasive commercial ultrasound probe to help locate your artery underneath the skin. After collecting enough pilot data from participants to ensure that the ultrasonic blood pressure monitor performs adequately for the validation procedures, we will begin the validation study.

Validation Study: Two trained observers will collect blood pressure measurements using a reference blood pressure cuff. These measurements will be compared to measurements collected at the same time from our ultrasonic patch. The ultrasonic patch will be placed on your neck, arm, or wrist at the beginning of the visit and will be removed at the end of the visit. We may also use a non-invasive commercial ultrasound probe to help locate your artery.

Three pairs of blood pressure measurements (1 measurement from the standard blood pressure cuff plus 1 measurement from the patch) will be collected in 3 different situations (9 pairs of measurements in total). The three situations are:

1) You will be asked to relax for 10 minutes in a calm, quiet environment at room temperature in the seated position. Then your blood pressure will be measured.

2) You will be secured to a tilt table with straps. You will rest quietly for 10 minutes in the lying position on the table. Your blood pressure will be measured. The tilt table will then be slowly raised to an angle of 60 degrees. In some people, this may cause blood pressure to drop; this is similar to what happens when you stand up. While you are upright, blood pressure will be measured at 1, 2, and 3 minutes of being upright. The table will then be lowered, and the straps will be removed.

3) After a period of time has passed, we will measure the blood pressure again to determine whether the ultrasonic patch remains accurate from the initial calibration.

The device representative, such as field engineers, will attend the blood pressure monitoring process to support the site personnel in operating the system.

In this study and at the request of the study doctor, a field engineer representative may:

1) Be present in the exam room to support the site personnel in operating the wearable continuous blood pressure monitor
2) Be present in the exam room to observe the use of the device and gather information and feedback from the doctor performing the procedure

The doctor or their designee will be present or nearby throughout the study duration. Please talk to your doctor if you have any questions.

How much time will each study procedure take, what is your total time commitment, and how long will the study last?

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The study will involve a screening visit, lasting approximately one hour, followed by a single study visit, which will be conducted on the same day following the screening visit. The study visit will last approximately one hour. The total time commitment will be about two hours on one day.

What risks are associated with this study?
Participation in this study may involve some added risks or discomforts. These include:

1) **Risks associated with the tilt table test:** The following temporary symptoms may occur during the tilt table test: low blood pressure and potentially associated symptoms including dizziness, lightheadedness, headache, neck pain, nausea, palpitations or change in heart rate, visual changes, cognitive changes, or syncope (fainting). If any of these symptoms cause you to be uncomfortable, the tilt table bed can be quickly lowered upon your request or the investigator's discretion. Lowering the table will improve the low blood pressure, which will result in resolution of any of these symptoms. You will be secured to the tilt table using straps and will be supported with a footrest so that falls cannot occur. The chance of these symptoms occurring during the tilt table test is similar to the risk that you experience in everyday life while standing upright.

2) **Risks associated with the device include**:

   A) Risks of ultrasound energy: The device delivers ultrasound into tissue and receives the echo signals. The motion of blood vessel walls can be tracked by analyzing these echoes. Since the ultrasound is a type of mechanical vibration, it will induce heat during reflections. The generated heat may cause mild discomfort. If you request removal of the device, it can be removed at any time.

   B) Risks of high voltage circuit: A 100 voltage AC source will be used to power the device. If this device were not properly insulated, it could cause a risk of electric shock. To prevent this risk, all electrodes in the device are encapsulated with insulating materials. The insulating materials are made to withstand approximately 10 times higher voltage than the electrodes.

   C) Risk of adhesive materials: The adhesive used to place the sensor on the skin may cause mild skin irritation or discomfort.

3) Risk of loss of confidentiality:
In compliance with HIPAA regulations, all records generated as part of your enrollment in the study are considered confidential. To protect confidentiality, you will be assigned a random coded identification number with no association to your identity as a participant. With these procedures, your name or personal identifying information (e.g., telephone number, address, date of birth) will never be used or recorded in analyses of data and are never associated with electronically transferred data or applied to subsequent reports of the scientific data in publications.

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Any files containing identifying personal health information (PHI) will be kept in a locked file cabinet located in Dr. Litvan's office along with the original signed informed consent form. You will be given copies of the signed original forms and the "Experimental Subject's Bill of Rights." This information will also be recorded into an encrypted electronic database.

Data will be stored on encrypted computer media and will be secured in a locked storage area at the clinical research office. Only the principal investigator, co-investigators, research coordinator, and database manager have password-protected access to the section of the database containing personal identifying information regarding the subject. Adverse event reports will use the unique identifying number and will not use your name. All electronic information will be stored in a secure password protected database. Paper files will be stored in locked cabinets, and staff will handle data in accordance with HIPAA guidelines as detailed above

Because this is a research study, there may be some unknown risks that are currently unforeseeable. You will be informed of any significant new findings.

What are the alternatives to participating in this study?
The alternatives to participation in this study are monitoring your blood pressure with a standard handheld or electronic blood pressure cuff. There are commercially available devices for continuous blood pressure monitoring, although they do not use ultrasound technology. No treatment will be provided or withheld during this study.

What benefits can be reasonably expected?
There is no direct benefit to you from these procedures. You may learn more about your own blood pressure changes. The investigators expect to learn more about using this device for continuous blood pressure monitoring and orthostatic hypotension from this investigation.

Can you choose to not participate or withdraw from the study without penalty or loss of benefits?
Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are entitled. If you decide that you no longer wish to continue in this study, you will be requested to: notify the investigator.
You will be told if any important new information is found during the course of this study that may affect your wanting to continue.

Can you be withdrawn from the study without your consent?
You may be withdrawn from the study if the investigators believe that it is in your best medical interest. You may also be withdrawn from the study if you do not follow the instructions given you by the study personnel.

Will you be compensated for participating in this study?
There will not be any monetary compensation provided for your participation in this study.

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Are there any costs associated with participating in this study?
There will be no cost to you for participating in this study. Parking costs will be provided.

What if you are injured as a direct result of being in this study?
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) for more information about this, to inquire about your rights as a research subject or to report research-related problems.

What about your confidentiality?
Research records will be kept confidential to the extent allowed by law. Paper documents related to the study will be kept in a locked room in the investigator's office. Electronic files related to this study will be kept on a secure, password-protected database. A report of the results of this study may be published, but your personal information (name, etc.) will not be disclosed in these documents. Research records may be reviewed by the study monitors and coordinators, the governing health authorities, the FDA. The UCSD Institutional Review Board may review research records.

Under California law, we must report information about known or reasonably suspected incidents of abuse or neglect of a child, dependent adult or elder including physical, sexual, emotional, and financial abuse or neglect. If any investigator has or is given such information, he or she may be required to report such information to the appropriate authorities.

Who can you call if you have questions?
Dr. Litvan and/or Dr. Longardner has explained this study to you and answered your questions. If you have other questions or research-related problems, you may reach Dr. Litvan at ilitvan@health.ucsd.edu or Dr. Longardner at klongardner@health.ucsd.edu.

You may call the Human Research Protections Program Office at 858-246-HRPP (858-246-4777) to inquire about your rights as a research subject or to report research-related problems.

Your Signature and Consent
You have received a copy of this consent document and a copy of the "Experimental Subject's Bill of Rights" to keep.

You agree to participate.

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Subject's signature Date

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