Official Title: Preliminary Studies to Test the Effects of Ambulatory Voice Biofeedback: Study 2
NCT Number: 03416868
Date: August 14th, 2024

Study Protocol:
Study Two will involve 48 total patients (20 with phonotraumatic VH and 20 with non-phonotraumatic VH + potential 20% drop out rate), each handled as a single subject design to test if large changes in voicing occur during AVB (acquisition) and the days post-AVB (retention). This experimental design is best suited for the study since (1) AVB can only be effective via an individualized approach to therapy and (2) we aim to demonstrate improvement with AVB across subjects who will have different measures as biofeedback targets. To be offered participation, each patient must successfully complete approximately one week of pre-therapy ambulatory data (acquired from protocol 2011P002376) and will need to demonstrate that the average behavior of a particular vocal function measure deviates by at least 1 standard deviation from normative values.
Throughout the first voice therapy session, the VHM will be worn with the goal of establishing a significant change in a voiced feature associated with perceptually improved voicing per the SLP. The SLP will use the VHM's real-time summary feedback to assess if improved voicing is significantly different than baseline. First, the baseline threshold will be based on 85th and/or 15th percentiles of measures from baseline that were >1 standard deviation away from out normative database. Second, the improved voicing must be over 90% compliant for at least 1 feature.

During the first therapy session, once the clinician has established that the patient can modify their voicing the patient will qualify for ambulatory monitoring without AVB the following week. Of note, patients will have already been trained on VHM use without AVB in the 2011P002376 protocol and completed a week of monitoring. After the first voice therapy session, each patient will begin monitoring without AVB in daily life. There will be no feedback in the patient's daily life so that we can evaluate if the patient can improve their voicing outside the therapy session without feedback.

The patient will receive monitoring with AVB during their second voice therapy session and subsequent monitoring in daily life. Starting in the second therapy session, the SLP will review the patient's performance over the previous week. The patient will be trained on using, and begin receiving, feedback for the last half of their therapy session. The training will include presenting how the biofeedback parameter is affected by their success. The patient will be asked to produce the targeted vocal behavior using negative practice in which s/he will be asked to purposefully perform a voicing task correctly and incorrectly to experience biofeedback cueing. The AVB will be provided throughout the second half of the first therapy session so that the patient can have practical training on its use and the clinician can ensure the AVB is tracking with improved voicing appropriately. During the ambulatory voice recordings, the patient will receive feedback on all 4 days of monitoring. During the week that the patient receives feedback, starting after this second therapy session, Dr. Van Stan will set up the VHM to provide feedback.
Starting in the third therapy session, the SLP will review the patient's performance over the previous week. If the patient did not respond to the feedback during week 2 monitoring, the study will stop for the patient and they will be paid for two voice therapy sessions and 8 days of monitoring (4 days per week). If the patient did responded to the feedback, they will qualify to continue the study during their third therapy session and in daily life the following week. The patient will be monitored during the third therapy session and for 4 days the subsequent week without the feedback. The purpose of the third week of monitoring is to see if the patient can retain their vocal improvements without the feedback.
The schedule of ambulatory monitoring time within each therapy week will be: 20 minutes of accumulated phonation time after the therapy session (Day 1), 40 minutes of phonation time for each of the next consecutive two days (Days 2 and 3), and 40 minutes of phonation time for the day before the patient's subsequent voice therapy session (Day 4). AVB will be provided during all days only during week 2. The specific AVB used will depend upon patient preference (e.g., some patients may find the frequent vibrotactile cueing of immediate feedback to be too distracting at their job). Throughout the study, subjects may be prompted to take a picture of their neck with the smartphone to document correct placement of the accelerometer.

TABLE II. Study 2 time points and associated visits/procedures.

Treatment Week 1	Treatment Week 2	Treatment Week 3
MGH Voice Center Investigator places VHM before voice therapy, voice therapy session is recorded, recording is uploaded onto Voice Center database, VHM reattached to subject, Day 1 recording begins	MGH Voice Center Investigator places VHM before voice therapy, voice therapy session is recorded. Subject will be trained to use and get biofeedback during therapy. Recording is uploaded onto Voice Center database, VHM reattached to subject, Day 1 recording begins	MGH Voice Center Investigator places VHM before voice therapy session 3, voice therapy session is recorded, recording is uploaded onto Voice Center database, VHM reattached to subject, Day 1 recording begins
Daily life Day 1 recording without feedback starts immediately after voice therapy. Wear VHM until record 20 minutes of voicing.	Daily life Day 1 recording with feedback starts immediately after voice therapy. Wear VHM until record 20 minutes of voicing.	Daily life Day 1 recording without feedback starts immediately after voice therapy. Wear VHM until record 20 minutes of voicing.
Day 2 and Day 3 recording without feedback will be two consecutive days post-Day1. Wear VHM until record 40 minutes of voicing	Day 2 and Day 3 recording with feedback will be two consecutive days post-Day 1. Wear VHM until record 40 minutes of voicing	Day 2 and Day 3 recording without feedback will be two consecutive days post-Day1. Wear VHM until record 40 minutes of voicing
Day 4 recording without feedback will be the day before Week 2's voice therapy session. Wear VHM until record 40 minutes of voicing.	Day 4 recording with feedback will be the day before the next voice therapy session. Wear VHM until record 40 minutes of voicing.	Day 4 recording without feedback will be the day before Week 2's voice therapy session. Wear VHM until record 40 minutes of voicing.

Statistical Analysis Plan:

Study Two will use one repeated measure ANOVA with 3 levels (pre-therapy days, AVB days pooled together (therapy week 2), retention days pooled together (after stopping AVB, therapy week 3) for the outcome variable of overall percentage compliance. The finding of interest is the main effect of "Level." Appropriate post hoc tests will be conducted on the main effects (if significance is achieved). It is hypothesized that the ANOVA will show, compared to pre-therapy, a significantly increased percentage compliance for all other levels. This result will demonstrate the expected large AVB effect that fades after AVB removal (smaller improvements during retention days than AVB days).

Mass General Brigham

Research Consent Form
General Consent Form Template
Version Date: November 2022

Subject Name:

MRN or DOB:

Subject Identification

Protocol Title: Preliminary studies to test the effect of ambulatory voice biofeedback in a small groups of patients with vocal hyperfunction
Subtitle: Study 2

Principal Investigator: Jarrad Van Stan, PhD, CCC-SLP

Site Principal Investigator:

Description of Subject Population: Adult Subject

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

We are asking you to be in a research study. This form will tell you what you should expect if you agree to be in the study. You will find more information about each of the following points later in this form.

It is your decision whether or not to join the study. We are asking you to be in this study because you were diagnosed with vocal fold nodules, polyps, or muscle tension dysphonia, are between 18-65 years old, and have successfully completed 1 week of voice monitoring in a previous research protocol (2011P002376). We are doing the research to determine how voice-related biofeedback provided in daily life—feedback based on your vocal behavior and delivered by vibration of or visual presentation on a smartwatch, smartphone—affects your ability to learn new therapeutic vocal behaviors and use them throughout the day. If you agree, you will receive standard voice therapy where the first week will include ambulatory monitoring without biofeedback, the second week will include ambulatory monitoring with biofeedback, and the

third week will include ambulatory monitoring without biofeedback. You will be in the study for 3 weeks if you decide to stay for the whole study.

The main risks of being in the study are skin irritation from the double sided stick tape used to adhere the sensor onto your neck, annoyance due to the biofeedback.

You might benefit from being in the study because traditional voice therapy and ambulatory voice biofeedback have been shown in previous work to improve vocal function.

If you decide not to be in the study, another thing that might help your condition is traditional voice therapy without biofeedback.

You will be paid up to $660 for taking part in this research study. You will find more information about the payment amount for each visit and a plan if you do not complete all study visits later in this form.

You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Jarrad Van Stan, PhD, CCC-SLP the person in charge of this research study. You can call him/her at 617-643-8410, Monday through Friday, from 8 am until 5 pm. You can also page him at 617-724- 5700 (ID 23979), 24 hours per day, 7 days per week, with questions about this research study.

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Why is this research study being done?

We are doing this study to determine how voice-related biofeedback provided in daily life – feedback received by vibration of a smartwatch based on your vocal behavior - affects your ability to learn new therapeutic vocal behaviors and use them throughout the day.

The study will use a device called the Voice Health Monitor (VHM). The VHM is a research device that records your voice through your neck skin vibrations. The sensor is an accelerometer which analyzes the vibration of your neck skin so that speech is not intelligible. This device is not approved by the U.S. Food and Drug administration (FDA). This means that the VHM can only be used in research studies.

This study is being done to see if the VHM is capable of helping subjects with vocal fold nodules, polyps, or muscle tension dysphonia learn how to carry over newly learned vocal behaviors from the voice therapy session into daily life.

We are asking you to take part in this research study because you have been diagnosed with vocal fold nodules, polyps, or muscle tension dysphonia and successfully completed a week of voice monitoring before starting voice therapy. About 48 subjects will take part in this study.

The National Institute of Health (NIH) is paying for this research to be done.

Dr. Robert Hillman, the Co-Investigator on this study, has a financial interest in InnoVoyce LLC, a company focused on developing and commercializing technologies for the prevention, diagnosis and treatment of voice-related disorders. In accordance with Partners HealthCare's conflict of interest policies, the Partners Office for Interactions with Industry has reviewed Dr. Hillman’s financial interest in the company and has determined that the interest creates no significant risk to the welfare of participants in this study or to the integrity of the research. If you would like more information about this, please contact the Partners Office for Interactions with Industry at 857-282-2024.

Who will take part in this research?

We are asking you to take part in this research study because you have been diagnosed with vocal fold nodules, polyps, or muscle tension dysphonia and successfully completed a week of voice monitoring before starting voice therapy. About 48 subjects will take part in this study.

The National Institute of Health (NIH) is paying for this research to be done.

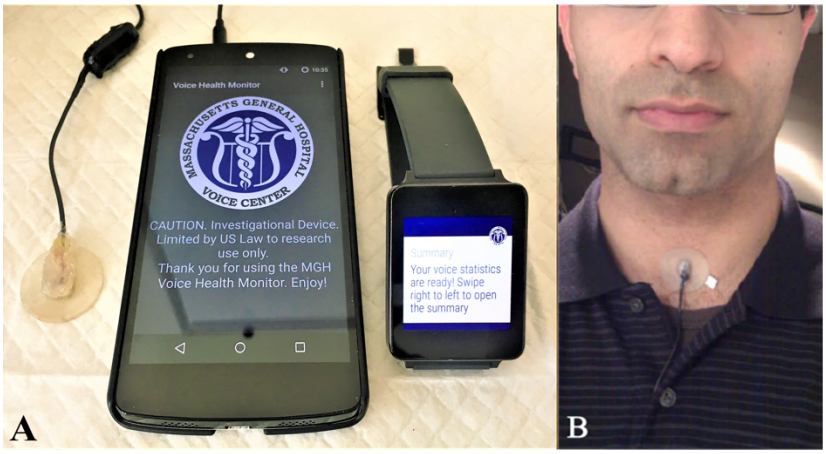
What will happen in this research study?

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

All visits will include an in-person visit to the MGH Voice Center coordinated with your voice therapy session and week of ambulatory voice monitoring (4 days of recording your voice during daily life). Throughout the study, subjects may be prompted to take a picture of their neck with the smartphone to document correct placement of the accelerometer.

The weekly visits to the MGH Voice Center will be combined with your therapy sessions:

- Each visit should last approximately 1 hour and 15 minutes and will begin 15 minutes before your therapy begins.
- The VHM app on the smartphone uses a small sensor attached to the front of your neck with medical grade double-sided tape. You can see a picture of the VHM below.
- Dr. Van Stan will place the sensor on your neck and mark its location (top and bottom) with a semi permanent marker so you have a reference of where to put it during the rest of the week (or should the sensor fall off and need replacement). The marks on the skin will fade away after approximately one week. He will also set up the VHM to record.
- We will teach you how to use the app to Start, Pause, and Stop the recording as well as reporting your level of vocal fatigue.
- You will wear the VHM throughout your voice therapy session.
- After your voice therapy session, Dr. Van Stan will upload your voice therapy data (which will take approximately 2-5 minutes) and give you the VHM back to wear in your daily life.



For the ambulatory voice monitoring, the recording should take no more than 10 hours to complete per day.

- Day 1 will start after your voice therapy session. You will wear the device for 20 minutes of talking time.
- Days 2 and 3 will start in the morning and are the two days after your voice therapy session. You will wear the device for 40 minutes of talking time.
- Day 4 will start in the morning the day before your next therapy session. You will wear the device for 40 minutes of talking time.
- When you reach the talking time limit each day, the device will vibrate, then show you a message stating that the recording has stopped and that you can remove the device.
- Dr. Van Stan will upload the 4 days of ambulatory recordings the day of your next voice therapy session (the day after Day 4).

Visit 1

This visit will be used to see if you qualify for ambulatory monitoring throughout voice therapy. To qualify for monitoring, the investigators will be trying to identify any measures that change in agreement with your voice therapist's judgement (i.e., a measure that changes when your therapist reports improve voicing). If we cannot find any measures that agree with your therapist's perception, the study will stop for you after this therapy session. You will be paid for the one voice therapy session. If we do find measures that agree with your therapist's perception, you will qualify for 4 days of monitoring the week after your first voice therapy session. There will be no feedback in your daily life so that we can evaluate if you can improve your voicing outside the therapy session without the feedback.

Visit 2

You will be receiving feedback during your second voice therapy session and subsequent monitoring in daily life. Starting in the second therapy session, your therapist will review your performance over the previous week with you. You will be trained on using, and begin receiving, feedback for the last half of your therapy session. Also, you will begin receiving biofeedback in your daily life after the therapy session. During the ambulatory voice recordings, you will receive feedback on all 4 days of monitoring. During the weeks you receive feedback, starting after your second therapy session, Dr. Van Stan will set up the VHM to provide feedback.

Visit 3

Starting in the third therapy session, your therapist will review your performance over the previous week. If the data do not show that you have responded to the feedback, the study will stop for you before this therapy session. You will be paid for two voice therapy sessions and 8 days of monitoring (4 days per week). If the data show that you have responded to the feedback, you will qualify to continue the study during your third therapy session and in daily life the

following week. You will be monitored during the third therapy session and for 4 days the subsequent week without the feedback. The purpose of the third week of monitoring is to see if you can retain your vocal improvements without the feedback.

Stopping the study early
Your participation in this study is entirely voluntary, and you may withdraw from the study even after signing this consent. The study doctor may have to take you out of the study. This may happen because:

1. We were unable to obtain usable information using the recording equipment during the therapy recording or ambulatory monitoring.
2. You were unable to wear the system for all of the days required.
3. There were difficulties scheduling study sessions.

Study information included in your medical record
A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example: list of allergies, results of standard blood tests done at the hospital labs).

Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

How may we use and share your samples and health information for other research?

The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

No. The research study we are doing is only a stepping stone in understanding **[condition].** Therefore, no information about the results of this research study or the results of your individual participation in the research study will be given to you or your doctor. Tests done for the research using your samples will not be useful in directing your medical treatment. The results of the tests will not be placed in your medical record.

What are the risks and possible discomforts from being in this research study?

Wearing the neck accelerometer may draw attention to you. You may cover it up with clothing (like a buttoned shirt, turtleneck, or a scarf) or jewelry. You may need to be careful when going to the restroom due to the wire attachment between the neck disk and the Samsung smartphone.

Removing the tape that holds the accelerometer on the neck may cause you brief discomfort similar to removing a Band-Aid. You may have a tiny bit of skin irritation where the sticky tape came off.

Being prompted about your vocal behavior throughout an entire day could be annoying depending upon your response to cueing and how often you are cued. This potential annoyance will be minimized since the biofeedback will be individualized according to your specific vocal difficulties.

If you were prompted to take pictures of your neck with the smartphone, it is possible that identifying features of the subject's face or photos of others may be inadvertently present in the picture. These pictures will only be used by MGH Voice Center study staff to confirm accurate placement of the accelerometer and will not be shared externally.

What are the possible benefits from being in this research study?

You may not benefit from taking part in this study. It is possible that your voice disorder will improve temporarily during the study. Others with vocal fold nodules, muscle tension dysphonia, or vocal fold polyp(s) may benefit in the future from what we learn in this study.

What other treatments or procedures are available for your condition?

You do not have to take part in this study to be treated for vocal fold nodules, polyps, or muscle tension dysphonia. Other treatments or procedures that are available to treat vocal fold nodules, polyps, or muscle tension dysphonia include:
Weekly voice therapy sessions without any feedback provided in your daily life.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

We will pay you $660 if you complete the study.

If you do not complete the study, we will pay you $25 for ambulatory recordings and $20 for the voice therapy recordings. If the device is returned without damage throughout the study and all recordings are successful, payment for each ambulatory recording will double to $50. Successful recording includes 20 minutes of phonation on therapy days, 40 minutes of phonation on all other days, and adherence to the study protocol.

If the device is not returned or lost, payment will only be issued for days in which data was transferred to the MGH Voice Center database.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if that happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

You will not be charged for any of the procedures done in this study.

Charges for any ongoing or routine medical care you receive outside this study will be billed to you or to your insurance company in the usual way. You will be responsible for any deductibles or co-payments required by your insurer for your routine medical care.

What happens if you are injured as a result of taking part in this research study

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you

may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National

Institutes of Health, and the Office for Human Research Protections), state agencies, and foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records

- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other:

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____
Print Name

_____ _____ _____
Subject Signature Date Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

Print Name

Signature of Study Doctor or Person Obtaining Consent

Date

Time (optional)

Consent Form Version: 6-30-2023