If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **The Placebo-controlled Effectiveness in NPH Shunting (PENS) Trial: Proof of Concept**

Application No.: **IRB00083576**

Principal Investigator: **Dr. Mark Luciano MD, PhD**
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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

While shunts have been used historically for treatment of patients with idiopathic Normal Pressure Hydrocephalus (iNPH) their efficacy has not been established in a randomized control trial, which is considered as the best form of evidence for any therapy. As a result, practice parameters vary widely amongst physicians who see patients with iNPH. This lack of solid evidence has hampered care of patients with iNPH since guidelines cannot be firmly recommended and potentially a large number of patients with iNPH are sub-optimally treated. Any surgical intervention has the potential to induce a significant placebo effect and hence improvement in gait and cognition after shunt surgery cannot be relied on as proof of efficacy. If the treating physicians are not blinded to the intervention it can subtly influence their assessments too. This study aims to address these challenges by blinding both the patient and evaluating personnel to the intervention, which for the purpose of this study is a functional shunt.

One of the aims of this study is to better understand the relationship between gene polymorphisms (natural genetic differences between people) and the likelihood of developing hydrocephalus and the likelihood of benefiting from a shunt.

People who have iNPH, are surgical candidates based on their clinical assessment and testing, and are planning to have shunt implantation are eligible for this study.

How many people will be in this study?

About 40 people, 60 years old and older, will be in this study, with 10 expected to participate at Johns Hopkins.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

Visit 1: If participants are deemed a candidate for shunt surgery post (post-LP), they will sign this consent and will undergo the baseline assessment of their gait, cognition, mood, activities of daily living, function, and bladder control by the following procedures:

- Gait: Your speed of walking will be assessed by how fast how you cover a distance of 10 meters. This is expected to take 5 minutes. Your gait test will be video recorded to ensure your speed and steps are measured correctly.
- Cognition: Your cognition will be assessed by 2 paper and pencil tests that assess different aspect of your memory, attention and speed of thinking. This is expected to take 15 minutes.
- Mood: Your mood will be assessed by a paper and pencil test. This is expected to take 10 minutes.
- Activities of Daily Living: You will be asked to fill out a questionnaire that asks you about activities you carry out during your daily life. This is expected to take 10 minutes.
- Function: Your function will be assessed using the modified Rankin Scale. This is expected to take 5 minutes
- Bladder control: This will be assessed by a questionnaire you will fill out. This is expected to take 5 minutes
- Physical exam
- Saliva collection

Visit 2/SURGERY: All participants enrolled in the study will have shunt implantation as standard of care for treatment of their iNPH. At the time of surgery half the patients will be randomized to have the shunt set in an open configuration at a setting of 4 on the shunt valve (Open shunt), while the other half will have the shunt at the highest setting of 8 that allows little CSF to flow through the shunt (Closed shunt). Neither the patient nor the evaluating personnel will know the shunt setting to maintain objectivity. The duration of this stay in the hospital is typically 2-3 days. Routine post-operative care will be given to both groups, both in the hospital and in follow-up clinic to remove the staples/sutures and monitor for any complications related to the surgery.

Visit 3/ONE MONTH: Participants will undergo the One Month Post-OP CT scan and will receive a telephone call from a study team member to discuss any new symptoms present and medications.

Visit 4/TWO MONTHS: Participants will receive a telephone call from a study team member to discuss any new symptoms present and medications.

Visit 5/FOUR MONTHS: Participants will repeat most of the baseline measurements from Visit 1 as detailed above. Some assessments may be done over the phone if participant is unable to return to the clinic. In addition, for participants in the closed shunt group, the shunt setting will now be changed to a setting of 4 by an independent study team member. Participants who are in the open shunt group may have their setting checked and may have the shunt setting adjusted, if clinically indicated.

Visit 6/FIVE MONTHS: Participants will undergo the Five Month Post-Op CT scan.

Visit 7/EIGHT MONTHS: Participants will repeat most of the baseline measurements from Visit 1 as detailed above. Some assessments may be done over the phone if participant is unable to return to the clinic. At this visit, the shunt settings in both groups will be adjusted as clinically indicated to the optimum setting.

Visit 8/TWELVE MONTHS/FINAL: Participants will again repeat most of the baseline measurements from Visit 1 as detailed above. Some assessments may be done over the phone if participant is unable to return to the clinic.

At every visit, if there are concerns based on the results of your gait, cognition, mood, or function assessments of significant impairments, we will contact your primary care physician, neurosurgeon, and neurologist to follow-up on those results.

Request to collect and store biospecimens for future research

Given that genetics research is developing at a very rapid pace, and new discoveries are made almost every day, we will keep your genetic information indefinitely. We may genotype your samples for genes other than those of interest in the current study, including genes that may not have yet been identified.

Please be assured that all of your identifying information will be removed from these samples. Master files containing your demographic information (e.g., age, sex, name, and identification number) will be kept in a secure location at the University of Utah that is separate from your saliva samples, which will be processed at Johns Hopkins University. Only investigators involved in the study and their research staff will have access to identifying information.

While we may share the results of our genetic analyses with other study investigators, we will never transfer ownership of your saliva/DNA samples to other parties. These tests are research-related only. We will not pass the results of the test on to you, as the results may not be clinically meaningful and are not being performed in a lab certified for clinical purposes.

You will be asked to abstain from eating, drinking or smoking for half an hour before the saliva collection. You will be provided with a kit to provide a small saliva sample. You will spit into a clear plastic tube until the collected saliva reaches the fill line (2 mL). The study coordinator will process the sample.

The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading *What happens to Data and Biospecimens that are collected in the study?*.

1) Will you allow us to store the saliva biospecimens we collect for this study for use in future research?

YES ☐ _____
Participant Initials

No ☐ _____
Participant Initials

How long will you be in the study?
You will be in this study for one year after the shunt has been implanted.

4. What are the risks or discomforts of the study?

Clinical interview and tests: You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Risk of Surgery: Everyone who is enrolled in the study, whether in the open shunt group or closed shunt group is subject to the standard risks associated with implantation of the shunt. Based on prior studies the expected risks are –

1) Bleeding into the brain at the time of surgery < 1%
2) Infection of the wound or shunt system <2%
3) Failure of the wound to heal <1%
4) Collection of fluid in the space between skull and brain 10%
5) Bleeding into the space between the skull and the brain 6%
6) Surgery to remove blood clots in the space between the skull and the brain 1%
7) Failure of the catheter inside the skull 4%
8) Failure of the catheter beyond that follows the shunt 4%
9) Failure of the valve 4%

Risks for the Closed Shunt Group:
There is a potential risk of worsening gait over the course of the first 4 months in the closed shunt group. If that leads to a fall that is clinically significant, it may result in medical or surgical complications.

The potential for increased shunt occlusion after four months of no flow is possible, though less likely with CSF. The risk of CSF leak due to shunt closure is minimal especially in these patients with normal pressure.

Confidentiality There is the risk that information about you may become known to people outside this study. We may disclose identifiable information about you as described in Section 11 of this form or in other cases. For example, the government including the FDA may see your information if it audits us, and the research team will voluntarily comply with Maryland disclosure laws and will tell the local or state authorities:

- if they suspect abuse or neglect of a child or dependent adult;
- if certain diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

There may be side effects and discomforts that are not yet known including those to the embryo and fetus if you were to become pregnant.

Because we will be collecting personal information, a potential risk is loss of privacy. For instance, one potential breach of confidentiality could involve genetic information that is linked to your personal information. The risk of breach of confidentiality will be minimized by ensuring that all information obtained during the study remains confidential and will be used solely for research purposes. All research staff will be closely supervised, trained, and reminded of the need to keep all information confidential. Additional measures will be taken to protect your confidentiality. All archival data will be stored on secure, encrypted, password-protected servers, to which only trained project staff have access. Your saliva sample will be kept in a separate secure location, identified only by a number, and separate from other identifying information you have provided (e.g., name, address). Finally, your name will never be associated with publications or presentations based upon this project.

5. Are there benefits to being in the study?

There is no direct benefit to you from being in this study. If you take part in this study, you may help others in the future.

6. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. The alternative to the type of treatment we are proposing is for you to have a shunt implanted as standard of care. You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

7. Will it cost you anything to be in this study?

All procedures, tests, drugs and devices in this study are part of your usual care and will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

8. Will you be paid if you join this study?

You will not be paid for your participation into the study.

9. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

10. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form, you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study, , including the video recordings of your gait test y. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

12. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You may be asked to give us a list of other health care providers that you use.

I agree that my study doctor and/or their representative may contact my other healthcare providers to request copies of my health care records that are required for my participation in this research.

Yes □ Signature _____ Date _____
No □ Signature _____ Date _____

13. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form, you will not give up any rights you have to seek compensation for injury.

14. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. Mark Luciano at 410-955-2259. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?
If you think you are injured or ill because of this study, call Dr. Mark Luciano at 410-955-2259 during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call Dr. Mark Luciano at 410-955-2259 during regular office hours and at 410-955-5000 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

15. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time
Signature of Participant	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

Assessment of capacity by research staff

I assessed _____ on _____ for the purpose of determining whether he/she is capable of understanding the purpose, nature, risks, benefits and alternatives (including non-participation) of the research, making a decision about participation, and understanding that the decision about participation in the research will involve no penalty or loss of benefits to which the patient is otherwise entitled, for the research project of "The Placebo-controlled Efficacy in NPH Shunting (PENS) Trial.. On the basis of this assessment I have arrived at the conclusion that:

___ A. This patient has this capacity at this time.
___ B. There is a question about this patient's capacity at this time.
___ C. This patient clearly lacks this capacity.

Print Name

_____

Signature _____ Date _____