

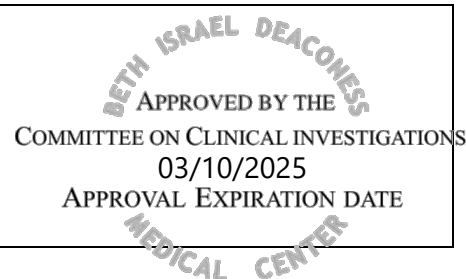


****For CCI Use Only****

**Approved by the Beth Israel Deaconess Medical Center
Committee on Clinical Investigations:**

Consent Approval Date: 03-11-2024

Protocol Number: 2022P000215



INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator: Rami Burstein
Protocol Number: 2022P000215

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you suffer from epilepsy (a brain disorder that causes seizures) that is resistant to treatment with drugs.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- Your participation is completely voluntary.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- Your refusal to participate will not result in any consequences or any loss of benefits that you are otherwise entitled to receive.
- You can ask all the questions you want before you decide.
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Beth Israel Deaconess Medical Center.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

**Why is this research being done?**

The purpose of this research is to determine whether BOTOX injections will reduce your seizure frequency and severity. BOTOX is a drug approved by the FDA for the treatment of chronic migraine. It has been in clinical use for over 20 years. We chose to test its effects on epilepsy because epilepsy and migraine have common

features so, are often treated with common drugs. If the study injection (BOTOX) helps reduce seizure severity and or frequency, the finding may lead to the development of a new and safe approach for the treatment of seizure.

How long will the research last and what will I need to do?

We expect that you will be in this research study for approximately 20 weeks (5 months) and you will attend 9 visits at BIDMC

First, you will be asked to fill a daily seizure diary for 8 weeks and will be asked questions about your medical history and medications to see if you qualify for the study. If you continue in the study, you will continue to fill in your seizure diary for the rest of the study. Second, you will have testing before the study injection that will be repeated two times after the injection. This will include having an electroencephalogram (EEG) and having a form of brain stimulation – transcranial magnetic stimulation (TMS) – to measure brain excitability (how your brain responds to stimulation). Third, you will receive the study injections. The injections are made in multiple locations under your skin. To cover your entire head, a total of 29 injections will be made just under your skin. This is a safe procedure we commonly use (given to millions of patients throughout the world) for the treatment of migraine in both children, adolescents and adults.

More detailed information about the study procedures can be found under **“DESCRIPTION OF STUDY DETAILS”**.

Is there any way being in this study could be harmful to me?

There are risks associated with BOTOX injections. These include weakness of neck muscles that develop after the injections. Since the study injection's effects last only 90 days, a full recovery to normal muscle strength is expected no later than 3 months after the injections. Overall, side effects are minimal as this drug does not enter the brain. Briefly, potential risks include temporary: double vision, dizziness, fatigue, numbness, allergic reaction, local infection, local bleeding, headache and/or neck pain, drop of eyelid or eyebrow, post treatment discomfort, swelling redness and bruising,

The most common side effect with TMS is headache. As many as 20-40% of people undergoing TMS report headaches. The most serious risk with TMS is a seizure, although this is rare and occurs in approximately 7 out of 100,000 TMS sessions. EEG is of minimal risk and should cause you no harm. There is a chance that you will experience some scalp irritation from the electrodes.

More detailed information about the risks can be found under **“RISKS AND DISCOMFORTS”**

Will being in this study help me in any way?



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

We cannot promise any benefits to you or others from your taking part in this research. However, *if BOTOX injections reduce your seizure frequency and severity, it may allow us to treat you and others better in the future.*

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

DETAILED INFORMATION SECTION

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part. You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF BIDMC AND INVESTIGATORS

This study is being conducted by Drs. Mo Shafi, Rami Burstein, Agustin Melo-Carrillo and their colleagues at BIDMC. It is funded by AbbVie/Allergan. Beth Israel Deaconess Medical Center (BIDMC), Rami Burstein, and Agustin Melo-Carrillo have additional interests in this research project or in the funding agency as follows:

Drs. Burstein and Melo-Carrillo are inventor of and has a patent on the novel approach of using BOTOX injections to reduce seizure severity – the topic of investigation in this study. BIDMC, Dr. Burstein and Dr. Melo-Carrillo may receive post-market royalty payments, as well as other payments from the potential sales of this product if it becomes marketed. The outcome of this study could affect the amount of royalties BIDMC and Drs. Burstein and Melo-Carrillo receives in the future. In addition, because BIDMC holds the patent on this technology, BIDMC may receive post-market royalty payments and could benefit from the outcome of this study if the results improved treatment of seizure.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Dr. Mouhsin Shafi, MD, PhD at [617] 667-0203.

PURPOSE

The main purpose of this study is to learn more about the use of Botox to treat focal seizures.

- The study injection reduces the ability of neurons (nerve cells) to communicate with each other. By doing so, it may be able to prevent the seizure from spreading. We would like to see if study injections into the scalp can:
 - Decrease focal seizures and,
 - Make focal seizures less likely to spread
- The drug involved in this study (BOTOX) is investigational. Botox is approved by the Food and Drug Administration (FDA) for treatment of chronic migraines, along with a number of other neurological and cosmetic conditions. In this study, the use of Botox is investigational, but will use same dose of Botox that the FDA has approved for the treatment of chronic migraines. Botox has not yet been proven to



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



be safe and/or effective for the treatment of focal seizures. The study treatment may work better, the same, or worse and may have less, more, and/or other risks compared to the clinical treatment options.

- In this study, the study injection is injected under the skin in your head, neck and shoulders.

We will use electroencephalogram (EEG) and transcranial magnetic stimulation (TMS) to measure your brain's excitability during this study. We will also use magnetic resonance imaging (MRI) if you have not completed an MRI scan in the past 3 years.

- **EEG** is used in routine clinical care to measure the brain's electrical activity. EEG involves placing a cap with electrodes (small metal discs) onto your head.
- **TMS** is a noninvasive way of stimulating the brain. TMS uses a magnetic field to cause changes in the brain activity. The TMS will be done with EEG to measure brain excitability. We will measure how your brain responds to the TMS before and after the BOTOX treatment.
- **MRI** is a noninvasive device that is used in routine clinical care to take pictures of the body. We will use the MRI to take pictures of your brain to help us target TMS to certain brain areas.

The device involved in this study, TMS, is investigational. This means that the study device is still being tested in research studies and is not approved by the Food and Drug Administration [FDA] for the way that it is being used in this study.

STUDY PARTICIPANTS

You have been asked to be in the study *because* study because you have focal seizures. In this research study we are trying to learn more about Botox treatment for people who have seizures like you. This treatment is being tried instead of more invasive treatments, such as surgery or vagal nerve stimulation.

Approximately 25 people will take part in this study at Beth Israel Deaconess Medical Center.

DESCRIPTION OF STUDY DETAILS

If you agree to be in this study, you will be in this research study for about 5 months – 2 months before treatment with the study injection and 3 months after the study injection.

After you sign the consent form, the following things will happen:

1. **Screening Procedures (1 study visit, Diary recording for 8 weeks):** Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. This visit will take approximately 1 ½ hours. For this research study, the screening procedures include:
 - A physical and neurological exam
 - Answering questions about your medical and seizure history
 - Questions to see if it is safe for you to have TMS. For example, you will be asked if you have any metal in your body. If it is not safe for you to have TMS, the study investigator may determine that



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



you can be in the study without completing the TMS with EEG testing.

- You will also be asked to record seizures and medications in a daily seizure diary application (seizuretracker) or in a paper seizure diary for 8 weeks prior to study treatment. You will be asked to share your seizure diary with the study team. If you are already using or choose to use the seizure tracker app, you will be asked to share your entries with the study team. You can share your entries in a few different ways.
 - First, you can share by using the “Valet” feature of the App. This allows you to share your diary entries with the study team for viewing only. You will be asked to share with this feature for the duration of the study.
 - Second, you can print a report from the App and share it with the study team.
 - Lastly, you can share your screen with the study team to allow them to view your entries.

In all cases, the study team will record the information that you share from the App in the study files. If you choose to use the App as your diary and are a new user, we will ask that you review the features of the App to learn about the features you can opt out of. For example, you can opt out of sharing your information with outside researchers. We will also ask that you do not choose to use the Alexa feature for the duration of the study.

It is very important that you fill in the seizure diary every day, whether you have a seizure on that day or not. If you are having trouble staying up-to-date with your seizure diary, please let a member of the study staff know immediately. If the initial 8 weeks of the seizure diary entries are not accurate or filled in daily, you may not be able to move into the treatment phase of the study. A member of the study team will call you periodically to check on your diary maintenance and diary entries.

At the end of 8 weeks, the research investigator will review your seizure diary to determine if you qualify for the treatment phase of the study. If the screening information shows that you cannot be in the research study, the research investigator will refer you back to your regular health care provider.

2. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures (please refer to the “Study Visit Schedule” below for an outline of study visits):

Baseline Testing (2 visits)

Baseline procedures will be done before you begin the treatment period. These will occur over 2 days. These procedures include a possible MRI, TMS with EEG measures followed by 24 hour EEG baseline measures, completion of a quality of life questionnaire and pregnancy testing if you are of child bearing potential.

MRI Scan (1-1.5 hours):

If you have had an MRI of your brain within the past 3 years, are in agreement that it can be used for



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

the study and we are able to get a copy of it, you will not have an MRI. If there is not an MRI that we can use, you will have an MRI. The MRI is used to help us locate specific brain regions during the TMS with EEG sessions.

- MRI is a method of taking pictures of the brain and of the blood flow in the brain, using a large magnet and radio signals. You will be asked to lie down on a platform that can slide into the magnet.
- An MRI imaging coil, which is made from special wires that are covered in plastic, will be placed around your head. Foam pads will be placed around your head to limit head movement during the scan.
- During the scan:
 - You will be asked to lie still on your back for about 30 minutes.
 - You will hear a loud knocking or hammering noise while the MRI is taking pictures, but the process itself will be painless. You will be given disposable earplugs to use to help make the noise less noticeable.
 - You will be in constant contact with the MRI technician through an intercom.
 - If at any time during the scan you feel too uncomfortable to continue, no matter what the reason, the procedure will be immediately stopped, and you will be removed from the MRI.
- If you have an MRI for this study, it is not an MRI to be used to diagnose problems; it is used for research purposes only. This means that the pictures will not be looked at by a radiologist. A radiologist is a doctor that looks at pictures taken by an MRI for potential diseases and damage.
- If an incidental finding is noted on the MRI, Dr. Mouhsin Shafi or a covering neurologist in the Berenson-Allen Center will review the scan. The neurologist will determine if the finding is in need of clinical follow-up. If this is the case, the neurologist will speak with you, will provide you with a letter describing the findings and need for follow-up and will be available to speak with your provider if you agree and give permission to do so.

For safety reasons, participants whose abdomen, shoulder, or hip circumference is greater than 180cm may not be able to have an MRI or may need to be excluded from the study.

The MRI procedure will take approximately 30 minutes plus time to change in and out of your regular clothes. The MRI may be done as part of the first visit based on availability and scheduling.

Transcranial Magnetic Stimulation (TMS with EEG) – (This visit will be 4-5 hours long):

If it has been determined that it is not safe for you to have TMS, this testing will not occur. The investigator will let you know if this is not being done. For this testing, you will come to the Berenson-Allen Center located at Beth Israel Deaconess Hospital for the TMS-EEG visit. There will be three TMS-EEG visits – one before the study injection and two after. The visits are identical and are described below.

We will use a copy of your clinical MRI scan to help guide the TMS. You will be seated comfortably in a chair for the TMS-EEG session. The following will happen for this assessment:

- EEG:



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

You will be seated in a chair and a cap will be placed on your head with electrodes (small discs) for the EEG. The electrodes will be filled with gel (not glue). You may need to wash your hair and skin once the electrodes are removed. This cap will remain on for the entire TMS testing. The EEG will allow us to measure how your brain reacts to the TMS and will allow us to measure any difference in your EEG following the BOTOX injection.

- Electromyography (EMG):

We will place electrodes (small discs) on your hand. These are used to record activity in your muscles and nerves during TMS. We will record signals from the electrodes while the EMG is in place.

- TMS:

- A tracker will be placed on your forehead. This will help the research team locate the spot for TMS stimulation using the MRI.
- The TMS coil will be placed firmly, but comfortably, against your scalp. The coil is made of wires that are covered in plastic and produces a magnetic field that will briefly affect your brain. The magnetic field is about the size of the tip of your finger.
- You will know that the magnetic field is on because you will hear a clicking noise. You might feel a tap or a pinch at the place that we are holding the coil. You may also feel a twitch in your face or scalp muscles. Each time the TMS is applied, we call this a "pulse."
- We will apply single pulses of TMS to different areas of your brain.
 - There are times that we will stimulate the part of your brain responsible for movement in your hand and your fingers will twitch when the magnetic pulse is given. This movement will be measured by EMG. This helps us measure the strength of TMS that we use to stimulate your brain.

Study staff will ask you to respond to a TMS side effect questionnaire before and after the TMS session. You will be asked to wear ear plugs and/or in-ear headphones during the TMS session.

24 hour EEG (1 hour for set-up and ½ hour for removal – this visit may happen on the same day as the TMS with EEG visit or on a separate day based on scheduling):

We will place electrodes (small discs) that have gel in them on your head with a special glue to hold them in place. Wires will come from the electrodes into a small recorder that you will wear on your waist. The electrodes will be covered up with a cap or gauze. You will be sent home with the EEG set-up in place. You will not be able to shower while you have the EEG on. You will return the following day and the EEG will be removed. You may need to wash your hair after the EEG is removed.

Study Treatment (1 visit, approximately 1/2 hour)

You will go to the anesthesia clinic at One Brookline Place to receive your study injection. The same dose that is used to inject BOTOX for migraine will be used for this study. The study medication will be injected in multiple locations just under your skin in your forehead, head, and neck. To cover the entire area, a



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



total of 29 injections will be made.

3. Monitoring/Follow-Up Procedures. Procedures performed to evaluate the effectiveness and safety of the research procedures are called “monitoring” or “follow-up” procedures. For this research study, the monitoring/follow-up procedures will happen over 12 weeks after the study injection.

- You will need to continue to keep a seizure diary for 12 weeks after the study injection
- The 24 hour EEG, TMS with EEG will be repeated approximately 3 and 8 weeks after the Botox (Up to 2 visits each time point – the TMS with EEG will take 4-5 hours and the 24 hour EEG will be 1 hour for set-up and ½ hour for removal)
- You will be asked to meet with study staff to review the study to complete the brief questionnaire about quality of life 12 weeks after the study injection. This visit should be about ½ - 1 hour long

In total, your participation in this study is expected to last approximately 20 weeks (5 months) and you will attend up to 9 visits at BIDMC.

Study Visit Schedule:

	Screening	Baseline	Treatment	Follow-Up 1	Follow-Up 2	Follow-Up 3
Study Visit Timeline	-8 to -12 Weeks	-1 to -4 Weeks	Day 1	3 Weeks	8 Weeks	12 Weeks
Consent	X					
Medical History & Physical/Neurological Exam	X					
Seizure and Medication Diary check -in	X	X	X	X	X	X
MRI (if needed)		X				
Pregnancy test		X				
24 hour EEG		X		X	X	
TMS with EEG		X		X	X	
Quality of Life Survey		X		X		X



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

Study Injection			X			
Adverse Event Check			X	X	X	X
Study summary and Neuro-QOL questionnaire						X

Individual Research Results

Your study doctor will disclose any clinically relevant research results to you, including any findings on your EEG, such as a seizure.

Most tests done in research studies are only for research and have no clear meaning for health care. The research testing done in this study is just a stepping stone to learning more about focal epilepsy.

While you should not expect to receive any results from the research testing, if we find that research results from your testing are of high medical importance, we may attempt to contact your medical provider to discuss the results. In some situations, follow up testing might be needed. You and your medical insurer may be responsible for the costs of these tests and any follow up care, including deductibles and co-payments. It is possible that you will never be contacted with individual research findings. This does not mean that you don't have or won't develop an important health problem.

Information and Biological Samples

Your information will be used and shared with the researchers involved in this study to conduct the research. The consent form provides information on who will have access to identifiable information during the study. We also want you to know that your information may be stripped of any identifiers (for example your name, medical record number or date of birth) and used for future research studies or distributed to another researcher for future research studies without additional informed consent. BIDMC researchers or other third party researchers may use your information in other scientific research, product testing or commercial development. It is unknown whether a product will ultimately be developed from the research described in this consent form or from any such work that may be performed by BIDMC or other third parties receiving your information. In signing this consent form, you are acknowledging and voluntarily consenting to the possibility that your information may be used for commercial purposes. For example, your information may be used to develop a new product or medical test to be sold. BIDMC and other researchers may benefit if this happens. There are no plans to pay you if your information is used for this purpose.

If your identifiers are removed, we will not be able to destroy or remove your information from distributed information. As part of this research program and as further explained in this form, information about your medical history may be provided to other researchers and/or outside collaborators.

RISKS AND DISCOMFORTS

As a result of your participation in this study, you are at risk for side effects listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



BOTOX Side Effects:

More common side effects: Dry mouth, discomfort or pain at the injection site, local bleeding, transient headache or neck pain, tiredness, eye problems: double vision, blurred vision, drooping eyelids, swelling of your eyelids, dry eyes; and drooping eyebrows.

Less Common side effects: infection, double vision, itching, skin rash.

Rare side effects: **Problems swallowing, speaking, or breathing** due to weakening of associated muscles. Allergic reactions including itching, rash, red itchy welts, wheezing, asthma symptoms, or dizziness or feeling faint.

PREGNANCY

Because of the effects of this study medication on a developing fetus is not known, you may not participate in this study if you are pregnant. In addition, it is possible that you could experience a seizure during the TMS (see "TMS Side Effects" below for details). This is rare and if it did occur, the type of seizure would most likely be what you typically experience with your seizures. TMS has not been known to cause a prolonged seizure (status epilepticus), but in the unlikely event that it did, this could be harmful for a fetus. If applicable, you will be required to take a pregnancy test to verify that you are not pregnant before the TMS and receiving your first dose of the study medication.

For the duration of the study, if you are engaged in sexual activity that could cause you or your partner(s) to become pregnant, you and your partner(s) must agree to use a highly effective method of birth control or abstain from sexual activity that could cause you or your partner(s) to become pregnant *[If appropriate, add language regarding avoiding pregnancy after completing study treatment].*

The methods of highly effective birth control for this study are below:

1. Contraceptive implant, such as Nexplanon
2. Levonorgestrel or copper intrauterine device (IUD), such as Mirena, Skyla, Kyleena, ParaGard or Liletta
3. Permanent female sterilization, such as tubal ligation, or Essure with confirmed tubal occlusion
4. Male partner(s) has had a vasectomy more than three months before study enrollment or with confirmation of successful occlusion
5. Combined hormonal contraceptives, such as the pill, patch or ring
6. Injectable contraception, such as Depo Provera

If you believe you have become pregnant while participating in this study, you must inform your study doctor immediately.

If you are a man capable of fathering children, you and your partner(s) must use highly effective birth control while participating in this study. For the purposes of this study, highly effective birth control means:

1. Consistent use of a condom AND
2. Your partner(s) must use an approved method of birth control as listed above.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



TMS Side Effects:

More Common Side Effects:

Pain:

As many as 20-40% of subjects undergoing TMS experience headaches, that is up to 4 in 10 participants. You may have pain, such as a headache, pain in your face or pain in your neck during or after TMS. This is managed with over the counter pain medications.

Redness:

You may have some redness on your head from the cap or tracker that you may wear during the TMS sessions. This redness is temporary.

Rare Side Effects:

Seizures:

If you have epilepsy, it is possible that you could experience a seizure during TMS; the risk is approximately 0.4-1.5% for patients with known epilepsy. This includes people who are on stable medications and have not had a recent seizure. Typically, the type of seizure a patient experiences while undergoing TMS is identical to those he or she usually experiences. TMS has never caused a prolonged seizure (known as status epilepticus) and has not caused a recurrence of a patient's seizure disorder (recurrent unprovoked seizures) outside the stimulation period.

Hearing problems:

TMS produces a loud clicking sound. It is possible that you could experience a temporary change in your hearing or ringing in your ears. You will have in-ear headphones or ear plugs in during the TMS. This will reduce the noise to prevent the risk of hearing problems. There is one report of someone who's hearing protection fell out who experienced permanent hearing loss from TMS. We will ask you to let us know immediately if:

- Your earplugs or in-ear headphones loosen, become detached or fall out.

You will be promptly referred for a hearing assessment if you experience hearing loss, ringing in the ear or ear fullness following completion of TMS.

Syncope (Fainting):

It is possible that you could faint during the TMS. This happens in less than 1% of people. Fainting can happen if you are anxious, nervous or have not eaten. You should immediately tell the study staff if you feel:

- Dizzy
- Lightheaded
- That you might pass out

If you have any of the above symptoms, the TMS will be stopped. You will be monitored until you are feeling better.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

**Electroencephalography (EEG):**

EEG is a safe and painless procedure for most people. You may experience some scalp irritation from the electrodes. If this happens, it will last a short time (a day or two).

Electromyography (EMG):

The sticky pads used for the test may cause skin irritation or redness. Taking the sticky pads off causes discomfort similar to when taking off a band-aid.

MRI:

MRI is a safe and painless procedure for most people. However, it is not safe for people who have pacemakers, ear implants, shrapnel injuries, or other types of metal or electric devices in their body, such persons will not be allowed to participate in the study. You must tell your doctor and the investigator about any operations you have had and any metal you may have in your body, so it can be decided if it is safe for you to proceed with the scan. We will also require that all people involved with the study remove all metal from their clothing and all metal objects from their pockets. No metal objects will be allowed into the magnet room at any time.

You may also experience mild psychological stress as a result of being in an MRI machine for the following reasons:

- Some people get a feeling of claustrophobia (fear of small places) while lying in the MRI. The sides and top of the scanner are very close to your face and body. If you suffer from claustrophobia, we ask that you do not participate in the study. The examiner and the technologist performing the scan will have voice contact with you constantly while you are in the MRI. If you feel the need to be removed from the MRI at any time, the scan will be stopped immediately.
- Lying in the MRI for an extended period of time may cause temporary discomfort. However, the investigators will make every effort to make you as comfortable as possible.
- The MRI makes loud banging noises as it takes pictures. Earplugs will be required to reduce this noise. With any radiofrequency (RF) coil, there is a risk of skin burns if the coil is used improperly. The MRI staff at Beth Israel Deaconess Medical Center is fully trained in the proper use of these devices. In normal operation, some subjects could experience warmth or heating. This should not be uncomfortable but please let the MRI staff know if it is.
- When very high-speed methods are used for imaging, some people experience a mild twitching sensation. This should not be uncomfortable but let the MRI staff know if you experience this sensation since we can modify the imaging method to eliminate it.

Questionnaire(s):

It is possible that there are questions that may make you feel uncomfortable. You can skip any questions that you do not wish to answer.

Loss of Confidentiality

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

**CONFIDENTIALITY**

Information learned about you during this research program will be maintained confidentially by the research staff as described in this form.

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, and by the drug manufacturer, AbbVie/Allergan, accreditation agencies, the Committee on Clinical Investigations, the Human Subjects Protection Office and others involved in research administration of the Beth Israel Deaconess Medical Center. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

MEDICAL RECORD

Information from this study will not be placed in your medical record.

POSSIBLE BENEFITS

It is unknown if there are any benefits to you from your taking part in this research study. Your epilepsy may get better, worse, or may stay the same during your participation in this study. We cannot promise any benefit to you. This research may help future children and adults with this type of epilepsy.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the following options: additional pharmacologic medications, surgery, vagal nerve stimulation, deep brain stimulation, responsive neurostimulation, ketogenic diet, or another clinical trial if available

This research study is not meant to diagnose or treat medical. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

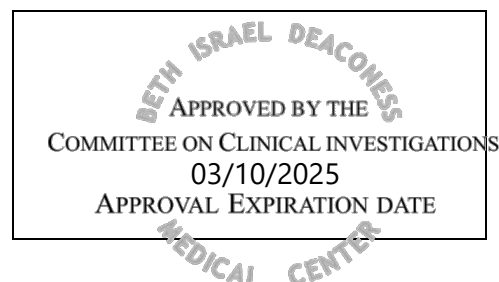
Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study. If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Beth Israel Deaconess Medical Center.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Beth Israel Deaconess Medical Center or the funding source may stop the study at any time.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



COSTS AND/OR PAYMENTS TO YOU

Costs Covered by Study

The procedures you receive are being performed only because you are participating in this research study. These activities will be paid for by the study and will not be billed to you or your health insurance company. There are no costs to you associated with this research study.

Payments to You:

If you complete all of the study visits, you will receive \$450 USD. You will receive \$50 for the screening visit, \$100 for the baseline visit(s), \$50 for the study injection visit, \$100 for follow-up visits 1 and 2, and \$50 for the final follow-up visit. If you are asked to have an MRI, you will receive an additional \$50. You will be paid for the study visits that you complete.

For this study, compensation will be provided through an electronic payment card (like a pre-paid debit card) called the ClinCard Program. The ClinCard Program is provided to BIDMC by a third-party company called GreenPhire. You will be issued a Greenphire ClinCard, which is a debit card that funds are loaded onto in connection with you taking part in this study. The study staff will provide you with additional information about how ClinCard works, including terms and conditions for the use of ClinCard. In order to complete your payments, Greenphire will need to process certain personal information about you: your name (required), birth date (required), address (required), and contact details (cell/mobile phone number and/or email address-optional for study related communications). This information will be collected from you by the staff in clinic and given to Greenphire. By agreeing to receive reimbursement for this study, you are authorizing the release of this information to Greenphire. By providing this information, Greenphire will be aware that you are enrolled in a clinical trial at BIDMC. Please allow up to three business days for payments to be credited to your ClinCard.

Any payments made to you may be taxable income to you. This does not include any payments you may receive to reimburse (pay you back) you for certain expenses like parking fees or travel. We are required to obtain your name and social security number for preparation and submission of Internal Revenue Service (IRS) Form 1099-Misc. You may receive an Internal Revenue Service Form 1099 from BIDMC if you receive more than \$600 or more in one calendar year for taking part in one or more research studies at BIDMC. Questions about your own tax status should be referred to your personal tax advisor.

You will be reimbursed for the following: transportation to your study visits. The amount of reimbursement will be up to \$40 per visit.

Cost of Research Related Injury:

If you are injured as a direct result of your participation in this study, you should contact the Investigator at the number provided under the section "Who to Call if You Have Questions" in this form. You will be offered the necessary care to treat your injury. We reserve the right to bill your insurance company or the sponsor, if appropriate, for the care you get for the injury. We will try to get these costs paid for, but you may be responsible for some of them. You may be responsible for all co-payments and deductibles required under your insurance. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

OTHER IMPORTANT INFORMATION

A description of this clinical trial will be available on 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.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

Description of Protected Health Information [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use and disclose health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests, and mental health records if applicable as well as any new information generated as part of this study. This is your Protected Health Information.

People/Groups at BIDMC Who Will Share and Use Your Protected Health Information

Your Protected Health Information may be shared with and used by investigators working on this study, including the supporting research team (such as research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, administrative assistants, and Greenphire), and may also be shared with and used by other health care providers at BIDMC who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research. Your Protected Health Information may also be shared with the members and staff of the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects, so that it can carry out its oversight responsibilities with respect to the study.

People/Groups Outside of BIDMC To Whom Your Protected Health Information Will Be Disclosed (Shared) and Who May Use Your Protected Health Information

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this research study:

- The funding source and/or sponsor of this study AbbVie/Allergan and, where applicable, the people and companies that the funding source and/or sponsor use to oversee, administer, or conduct the research (for example, clinical research organizations are companies that are sometimes hired by research sponsors to help manage and run a clinical research study)
- The other hospitals and medical centers taking part in this study and research collaborators at those institutions.
- Other research collaborators and supporting research team members taking part in this study
- Any external health care providers who provide services to you in connection with this research
- Laboratories not affiliated with BIDMC that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with BIDMC
- The members and staff of any other IRBs (beyond the BIDMC Committee on Clinical Investigations)



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



that oversee the research

- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

Purpose: Why We Are Using and Sharing Your Protected Health Information

The reason for using and sharing your Protected Health Information is to conduct and oversee the current, secondary, and future research described in this Informed Consent Document. There are many other reasons beyond the research for which BIDMC may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which BIDMC may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of BIDMC's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the BIDMC Notice of Privacy Practices.

No Expiration Date – Right to Withdraw Authorization

Your authorization for the use and disclosure of your Protected Health Information in this Study shall never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Rami Burstein, PhD, at Center for Life Science, room 649, 3 Blackfan Circle or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

Refusal to Sign

Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

Right to Access and Copy your PHI

If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215



Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that the Beth Israel Deaconess Medical Center has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

Signature of Subject or
Legally Authorized Representative
(Parent if the subject is a minor)

Date

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.



Subject's Name:
Title of Research Protocol: BOTOX effects on seizure severity and susceptibility
Principal Investigator's Name: Rami Burstein
Protocol #: 2022P000215

BETH ISRAEL DEACONESS APPROVED BY THE COMMITTEE ON CLINICAL INVESTIGATIONS 03/10/2025 APPROVAL EXPIRATION DATE MEDICAL CENTER
--

THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study. Signature of Witness: _____ Printed Name of Witness: _____ Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study. Signature of Witness: _____ Printed Name of Witness: _____ Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions. Signature of Interpreter: _____ Printed name of Interpreter: _____ Date: _____
