MedStar Research Institute

MedStar Health

Approval Notice
Amendment

20-Apr-2009

Washington Hospital Center
110 Irving St, NW, Ste 2A-66
Washington, DC 20010

Protocol Number:	**2008-380**
PI Name:	**Brian Walitt MD**
Protocol Title:	**Functional Magnetic Resonance Imaging as a Surrogate Measure of Fibromyalgia Symptoms**

Dear Brian Walitt MD,

The above-referenced **Amendment** submission was reviewed by **IRB # 1 Washington** via expedited review on **20-Apr-2009**.

The IRB approved the following modification(s): **addition of questionnaires and revised informed consent document**

The approval is valid through *20-Jan-2010*. Any modifications to the IRB-approved protocol and other supporting documents must be reviewed and approved by the IRB prior to implementation.
If the study will continue beyond the expiration date, please submit a continuation request form forty-five (45) days prior to the expiration date to allow the IRB sufficient time to review and approve the request.

Please refer to the Office of Research Integrity website to review the **Principal Investigator's Responsibilities** as a MedStar researcher on http://www. medstarresearch.org/Body.cfm?id=243.

If you have any questions, please contact me at 301-560-7339.

Thank you,

Jacqueline Steenbakker
Office of Research Integrity

Enclosure: Stamped Informed Consent Document
Stamped Questionnaires (pre-scan & post-scan)
Stamped Patient Global Assessment of Change Questionnaire

IRB number:	**Clinical Site IC Version:**
Project Title:	Functional Magnetic Resonance Imaging as a Surrogate Measure of Fibromyalgia Symptoms
Principal Investigator: Brian Walitt MD MPH	**Institution:** Washington Hospital Center

MedStar Research Institute Informed Consent for Clinical Research

INTRODUCTION

We invite you to take part in research study called *Functional Magnetic Resonance Imaging as a Surrogate Measure of Fibromyalgia Symptoms".* You were selected as a possible participant in this study because you have fibromyalgia. Please take your time to read this form, ask any questions you may have and make your decision. We encourage you to discuss your decision with your family, friends and your doctor(s).

WHAT IS THE PURPOSE OF THIS STUDY?

This study is being done to determine if a special type of magnetic resonance imaging (MRI) can be used to measure the symptoms of fibromyalgia. The pain of fibromyalgia is very difficult to measure and the cause of fibromyalgia is unknown. It appears that abnormal function of particular parts of the brain and spinal cord can cause and maintain the pain of fibromyalgia. It is possible to measure the function of these parts of the brain and spinal cord using a non-invasive technique called functional magnetic resonance imaging (fMRI) which uses magnets to take pictures of how the brain is working. By taking pictures of the brain with fMRI before and after interventions designed to positively and negatively change your fibromyalgia symptoms, we hope to determine how the activity of your brain and spinal cord change in relation to your symptoms. We hope to use these fMRI techniques to be able to determine if a person has fibromyalgia, to help determine if future therapies work, and to better understand the cause of the illness itself.

WHAT ELSE SHOULD I KNOW ABOUT THIS RESEARCH STUDY?

It is important that you read and understand several points that apply to all who take part in our studies:

- Taking part in the study is entirely voluntary and refusal to participate will not affect any rights or benefits you normally have;
- You may or may not benefit from taking part in the study, but knowledge may be gained from your participation that may help others; and
- You may stop being in the study at any time without any penalty or losing any of the benefits you would have normally received.

The nature of the study, the benefits, risks, discomforts and other information about the study are discussed further below. If any new information is learned, at any time during the research, which might affect your participation in the study, we will tell you. We urge you to ask any questions you have about this study with the staff members who explain it to you and with your own advisors prior to agreeing to participate.

WHO IS IN CHARGE OF THIS STUDY?

The investigator is Dr. Brian Walitt. The research is being sponsored by a grant from the MedStar Research Institute.

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Form Revision Date: 05/10/04

WHO CANNOT PARTICIPATE IN THIS STUDY?

You cannot be in this study if any of the following apply to you:

- Severe concomitant psychiatric illness as determined by psychiatric screening instruments or investigator judgment
- Significant suicide risk as determined by psychiatric screening instruments or investigator judgment
- Abuse of alcohol, benzodiazepines, or other drugs as demonstrated by psychiatric screening instruments
- Significant claustrophobia that will interfere with fMRI scanning
- Implantable metal devices or injuries that would interfere with fMRI scanning
- Self-reported inability to adhere to the study exercise protocol
- Severe medical health problems, to include cardiac, pulmonary, or rheumatic disease that will interfere with a participant's ability to successfully participate in the study intervention.
- Documented systemic autoimmune disease, including systemic lupus erythematosus, rheumatoid arthritis, Sjogren's Syndrome, inflammatory myositis, scleroderma, inflammatory bowel disease, and celiac sprue. Stable organ specific autoimmune disease, such as Hashimoto's, Graves', or myasthenia gravis will be allowed.
- Active malignancy. Basal cell carcinoma will be allowed.
- Pregnant or breastfeeding.
- Received experimental agent within last 30 days.
- Inability to stop or wean off, medications that have known central nervous system action.

These include: anti-depressants, anti-convulsants, narcotics and opiates, benzodiazepines, stimulants, muscle relaxants, buspirone, sodium oxybate, phenobarbital, systemic steroids, 5-HT agonists, and centrally-acting sleeping agents

WHAT IF I AM PRESENTLY PARTICIPATING IN ANOTHER RESEARCH STUDY?

Are you presently participating in any other research studies? Yes ☐ No ☐

If yes, please state which study(ies)_____

While participating in this study, you should not take part in any other research project without approval from the people in charge of each study. This is to protect you from possible injury arising from such things as extra blood drawing, extra x-rays, interaction of research drugs, or similar hazards.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About **8** people will take part in this study, worldwide. **8** people will be recruited at this site.

WHAT HAPPENS IF I AGREE TO BE IN THE STUDY?

The purpose of this study is to measure how the activity of your brain changes after particular changes in your life. Initially, you will be asked to come in for a screening visit. At this visit, you will be asked several questions, fill out some

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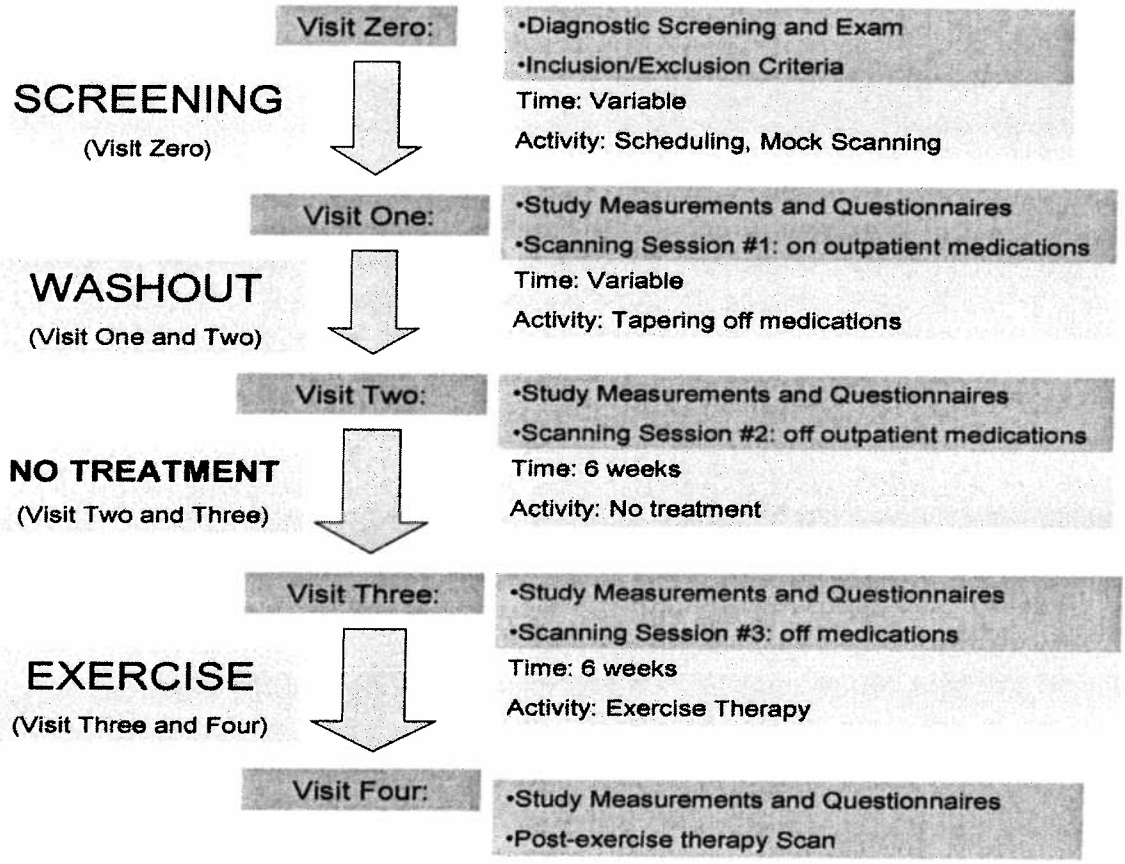
questionnaires, and be examined. You will be also undergo a mock scanning session, where you will be placed in a model of the scanning machine to be used in the study. This is done to ensure you can tolerate the scanning procedure. This is done to ensure that you do not find the space too tight or too loud for you to tolerate. If you are still interested in participating and meet all of the screening criteria, you will be scheduled for your first study visit.

Figure One: Summary of Study Schedule



At the first study visit, you will arrive in the morning at the study site. You will be asked to perform a series of questionnaires about your fibromyalgia symptoms. You will then undergo a procedure called 'subjective scaling'. In this procedure, we use a device called a digital compression unit (DC unit) to apply different amounts of pressure to the base of your thumbnail. We will ask you to rate how painful each of these pressures are. This information will be used to develop a personal pain scale for the research study. After the scaling is completed, you will be placed in the MRI scanner. In the scanner, you will undergo a number of scans. Some of the scans will be with you simply resting or watching television. We will also take scans while we apply pressure to your thumbnail with the DC unit so we can see how your

brain activity changes when you perceive pain from the DC unit. We will give you breaks during the scanning session. It is expected that the entire time in the scanner, with breaks, will be between 90 to 120 minutes.

After the first study visit, Dr Walitt will provide a schedule for you to taper off your fibromyalgia medications. At minimum, you will need to stop your medications for three 'half-lives' (the length of time required for half the dose of the medication to leave your body) before you can participate. Depending on the medications you are taking, it may take anywhere between 1 week to several months to stop your medications. The medications will be stopped slowly to reduce potential problems from withdrawal symptoms. You will likely have more problems with your symptoms as you come off of the medications. After you have stopped your medications, you will be scheduled for another scanning session. You will undergo the same questionnaires, same 'subjective scaling' with the DC unit, and the same MRI scans as described above.

After the second scanning visit, you will be scheduled for another scanning session 6 weeks later. During these six weeks, you will not be allowed to take any of your fibromyalgia medications to treat your fibromyalgia symptoms. Acetamenophen (Tylenol) and over-the-counter anti-inflammatories (such as ibuprofen [advil] or naprosyn [aleve]) can be used to help with your symptoms for the first 4 weeks but we will ask you to refrain from using any medications during the two weeks before the third scanning period. After the six weeks has passed, you will undergo a third scanning session that will be exactly the same as described above.

After the third scanning session, you will start an aerobic exercise regimen under the guidance of physical therapists at the National Rehabilitation Hospital. You will undergo a physical evaluation where measurements of your exercise capacity will be made and your body mechanics will be analyzed. If needed, the therapists will provide you with any equipment that they believe will make it more comfortable for you to exercise. After the initial evaluation, you will start the aerobic exercise regimen. It will take place three times each week for six weeks. Each session will begin with a 5 minute warm-up, followed by 20 minutes of moderate level aerobic exercise, and finish with a 5 minute cool down. The level of exercise will be enough to break a sweat but still low enough so that you could carry on a conversation while exercising. You will be able to choose the exercises you wish to perform, including exercise bicycle, therapeutic pool, treadmill, upper extremity 'bicycle', and walking. At the end of the program, you will undergo a final exercise assessment. At the completion of the exercise therapy, you will be scheduled for a final scanning session that will be exactly the same as described above. During the entire period of the exercise therapy, you will have to refrain from using medications to treat your fibromyalgia symptoms. Tylenol and over-the-counter anti-inflammatories can be used to help with your symptoms for the first 4 weeks of therapy but we will ask you to refrain from using any medications during the two weeks before the final scanning period. After the final scanning session, the research study will be complete.

This study requires you to refrain from using medications to treat your fibromyalgia symptoms. There is potential discomfort for you if you participate in this study. The study investigators realize that they are asking you to tolerate your symptoms without help as best you can throughout the study. However, if you find that you are unable to tolerate your symptoms, you may request to drop-out of the study into the RESCUE therapy protocol. This entails participation in Dr Walitt's outpatient clinic where individualized care will be provided to bring your symptoms under better control. A number of different modalities may be utilized, from reinstatement of prior medications, use of a range of medications selected to treat particular symptoms, intra-articular and myofascial trigger injections, and therapeutic consultations with a variety of subspecialists and therapists. This additional care will meet typical community standards and, therefore, be funded through your health insurance plan. The goal of the RESCUE therapy protocol is to stabilize your symptoms so you can resume care with your regular doctors.

At the end of each of the four study visits, a blood draw will be performed. A single 10cc tube of blood will be collected and placed into a research freezer. These samples will eventually be used to determine if your blood and immunological proteins change in a similar manner to your symptoms and your changes in brain function as measured by fMRI. These samples will not be used for genetic testing.

Please advise the researchers of any medications you are taking. In addition, if you are taking any over-the-counter drugs or herbal supplements which you have obtained from the drug store, grocery store, etc., you should advise the researchers.

The procedures that are experimental are:

- 'Subjective scaling' using a digital compression unit to apply pressure to the base of your thumbnail
- Functional Magnetic Resonance Imaging (fMRI)

The procedures that are not experimental are:

- History and Physical Examination
- Study Questionnaires
- Aerobic exercise therapy
- Blood draw

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for approximately 30 weeks.

The investigator may decide to take you off this study if it is believed to be in your best interest, you fail to follow instructions, new information becomes known about the safety of the study, or for other reasons the investigator or sponsor believes are important.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the investigator and your regular doctor first so they can help you decide what other options may be best for your medical care once you are off study.

If you suddenly withdraw from the study, we will be unable to provide you assistance with your fibromyalgia symptoms and we may not be able to use any of the information gathered from your participation.

WHAT ARE THE RISKS AND SIDE EFFECTS OF THIS STUDY?

If you decide to participate in this study, you should know there may be risks. You should discuss these with the investigator and/or your regular doctor and you are encouraged to speak with your family and friends about any potential risks before making a decision. Potential risks and side effects related to this study include:

Risks and side effects ***that may occur*** include:

- Withdrawal symptoms from stopping your current fibromyalgia medications.
- Discomfort from fibromyalgia symptoms that may occur from stopping your medications over the course of the study.
- Muscle soreness and discomfort related to participating in exercise therapy.
- Discomfort from undergoing functional magnetic imaging. This may include discomfort related to being in an enclosed space for a prolonged period of time (claustrophobia), discomfort from laying still for a prolonged period of time, and discomfort from the noise of the scanner.
- Discomfort from pain stimulus testing to the base of the thumbnail.
- Discomfort, discoloration, or bleeding at the site of the blood draw.

Risks and side effects ***that are less likely to occur*** include:

- Soft tissue injury, such as muscle strain tear, during exercise

Risks and side effects ***that rarely occur*** include:

- None

Please tell the investigator about all medications including over the counter drugs or herbal supplement you are taking, even if you don't think they are important.

Avoidance of Pregnancy: Because the results of the study may be affected by pregnancy, you should not become pregnant or nurse a baby while taking part in this study. If you or your partner could become pregnant, you should ask about counseling and more information about preventing pregnancy. If you do become pregnant during the study or if you father a child during the study, you should immediately notify Dr Brian Walitt at (202) 877-6274.

There may also be risks and side effects, other than those listed above that we cannot predict. Many side effects go away shortly after the MRI and exercise procedures are stopped, but in some cases side effects can be serious, long lasting and/or life threatening. If you have any unwanted side effects, you should ask the investigator whether there are any medications or other things that may be done to make the side effect less uncomfortable.

For more information about risks and side effects, please ask Dr Brian Walitt.

FOR STUDIES INVOLVING THE CENTER OF FUNCTIONAL AND MOLECULAR IMAGING:

Throughout the study, we will tell you about new information we receive about treatments that may be appropriate for you and any information that may affect your interest in remaining in the study. The investigators for this project are not trained to perform radiological diagnosis, and the scans performed are not optimized to find abnormalities. The investigators are not responsible for failure to find existing abnormalities in your MRI scans. However, on occasion the investigator may notice a finding on a MRI scan that seems abnormal. When this occurs, a neurologist will be consulted as to whether the finding merits further investigation, in which case the investigator or the consulting neurologist would contact you and your primary care physician to inform you of the finding. The decision as to whether to proceed with further examination lies with you and your physician. The investigators, the consulting neuroradiologist or neurologist, and Georgetown are not responsible for any examination or treatment that you undertake based upon these findings.

Because images in this study do not comprise a proper clinical MRI series, these images will not be made available for diagnostic purposes.

FOR FEMALES PARTICIPATING IN FMRI STUDIES ONLY:

__ I am a female of child-bearing potential and I am not pregnant. I agree to take a free pregnancy test to confirm that I am not pregnant.
__ I am not of child-bearing potential.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

You may or may not get any direct benefit from being in this study. We cannot promise that you will experience any benefits from participating in this study. We hope the information learned from this study will benefit others in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

- Continue with your current medical care.
- You always have the option to not be in this study or to refuse any medical treatment.

WHAT ABOUT CONFIDENTIALITY?

Your personal health information (PHI) will be kept private to the extent allowed by law. You will not be identified by name in any publications resulting from this study. You will be asked to sign a separate form that will give permission to the investigator, the sponsor, and certain other people, agencies or entities to look at and review the records related to this study including your personal health information and the information discovered during this study. If you do not wish to sign this permission form you will not be allowed to participate in this study. Participants that are found to have suicidal ideations during the screening process will be referred for appropriate evaluation and treatment.

WILL I BE PAID FOR PARTICIPATING IN THIS STUDY?

You will be paid for being in this study. You will be paid $10/hour for each of the 4 study visits that require use of the digital compression unit and fMRI scanning. You will be paid $10 per visit for your time during each of the exercise therapy visits.

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You will be reimbursed for expenses related to travel and parking for both the study and the exercise therapy visits. Materials and information obtained from you in this research may be used for commercial or non-commercial purposes. It is the policy of Washington Hospital Center, Georgetown University Hospital, MedStar Research Institute, MedStar Health, Inc. and its affiliated entities not to provide financial compensation to you should this occur.

WHAT ARE THE COSTS?

You do not have to pay anything to be in this study. However, if taking part in this study leads to procedures or care not included in the study, it may lead to added costs for you or your insurance company. You will not be charged for the MRI scans or exercise therapy that are part of this research study.

However, you, or your insurance company, will be charged for any other portion of your care that is considered standard of care. You may be responsible for any co-payments and deductibles that are standard for your insurance coverage. This may include: medications and procedures used to treat pain if you decide to withdraw from the study.

WHAT IF I'M INJURED OR BECOME ILL DURING THE STUDY?

We will make every effort to prevent injuries and illness from being in the study. In the case of an injury, illnesses, or other harm occurring during, or resulting from, the study, emergency medical treatment is available but will be given at the usual charge by the Washington Hospital Center or Georgetown University Hospital. You or your insurance company will be charged for any continuing medical care and/or hospitalization that are not a part of the study.

If you have an injury or illnesses occurring during, or resulting from the study, you, your medical insurance, a third-party payer, or a government program you've enrolled will be expected to provide coverage for your medical care. MedStar Research Institute does not intend to provide reimbursement for costs of medical treatment for injury or illness if such costs are not covered by your medical insurance, a third-party, or governmental programs providing such coverage.

No funds have been set aside, by the Washington Hospital Center, Georgetown University Hospital, the MedStar Research Institute, MedStar Health, or its affiliated entities to repay you in case of injury, illness, or other harm occurring during, or resulting from the study and their current policies do not provide for payments for lost wages, cost of pain and suffering, or additional expenses. By agreeing to this you do not give up your rights to seek compensation in the courts.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

- You have the right to be told about the nature and purpose of the study;
- You have the right to be given an explanation of the exactly what will be done in the study and given a description of potential risks, discomforts, or benefits that can reasonably be expected;
- You have the right to be informed of any appropriate alternatives to the study, including, if appropriate, any drugs or devices that might help you, along with their potential risks, discomforts and benefits;
- You have the right to ask any questions you may have about the study;
- You have the right to decide whether or not to be in the study without anyone misleading or deceiving you; and
- You have the right to receive a copy of this consent form.

IRB number:	**Clinical Site IC Version:**
Project Title:	Functional Magnetic Resonance Imaging as a Surrogate Measure of Fibromyalgia Symptoms
Principal Investigator: Brian Walitt MD MPH	**Institution:** Washington Hospital Center

By signing this form, you will not give up any legal rights you may have as a research participant. You may choose not to take part in or leave the study at any time. If you choose to not take part in or to leave the study, your regular care will not be affected and you will not lose any of the benefits you would have received normally. We will tell you about new information that may affect your health, welfare, or willingness to be in this study.

WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the investigator, Dr Brian Walitt, at (202)877-6274.If you are having a medical emergency, you should call 911 or go directly to the nearest emergency room.

For questions about your rights as a research participant, contact the MedStar Research Institute. Direct your questions to the Office of Regulatory Affairs at:

Address:	MedStar Research Institute 6495 New Hampshire Avenue Suite 201 Hyattsville, MD 20783	Telephone: Toll Free: Fax	(301) 560-7339 (800) 793-7175 (301) 560-7336

SIGNATURES

As a representative of this study, I have explained the purpose, the procedures, the possible benefits and risks that are involved in this research study. Any questions that have been raised have been answered to the individual's satisfaction.

Signature of Person Obtaining Consent _____ Date of Signature _____

I, the undersigned have been informed about this study's purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to be in this study. I am free to stop being in the study at any time without need to justify my decision and if I stop being in the study I understand it will not in any way affect my future treatment or medical management. I agree to cooperate with (name of principal investigator) and the research staff and to tell them immediately if I experience any unexpected or unusual symptoms.

Participant's Signature _____ Date of Signature _____

Signature of Witness _____ Date of Signature _____

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Form Revision Date: 05/10/04

Pre-Scan Symptom Checklist
Study FM01: FMRI in Fibromyalgia

Patient #:_____ Date:_____
Time:_____

1. At this point in time, how bad is your pain?

No Pain •___|___|___|___|___|___|___|___|___|___• Very Severe Pain

2. At this point in time, how tired are you?

No Tiredness •___|___|___|___|___|___|___|___|___|___• Very Tired

3. At this point in time, how difficult is it to think and concentrate?

Not Difficult •___|___|___|___|___|___|___|___|___|___• Very Difficult

4. At this point in time, how depressed or blue do you feel?

Not Depressed •___|___|___|___|___|___|___|___|___|___• Very Depressed

5. At this point in time, how anxious do you feel?

Not Anxious •___|___|___|___|___|___|___|___|___|___• Very Anxious

Post-Scan Symptom Checklist
Study FM01: FMRI in Fibromyalgia

Patient #:_____ Date:_____
Time:_____

1. At this point in time, how bad is your pain?

No Pain •___|___|___|___|___|___|___|___|___|___• Very Severe Pain

2. At this point in time, how tired are you?

No Tiredness •___|___|___|___|___|___|___|___|___|___• Very Tired

3. At this point in time, how difficult is it to think and concentrate?

Not Difficult •___|___|___|___|___|___|___|___|___|___• Very Difficult

4. At this point in time, how depressed or blue do you feel?

Not Depressed •___|___|___|___|___|___|___|___|___|___• Very Depressed

5. At this point in time, how anxious do you feel?

Not Anxious •___|___|___|___|___|___|___|___|___|___• Very Anxious

Participant Global Impression of Change
Study FM01: FMRI in Fibromyalgia

Patient #:_____ Date:_____
Time:_____

Since the last study visit, how has your fibromyalgia symptoms changed overall?

☐ Very much worse
☐ Much worse
☐ Minimally worse
☐ No change
☐ Minimally better
☐ Much better
☐ Very much better